Clinical trial results:
A Randomized, International, Double-Blinded (With In-House Blinding), Controlled With GARDASIL™, Dose-Ranging, Tolerability, Immunogenicity, and Efficacy Study of a Multivalent Human Papillomavirus (HPV) L1 Virus-Like Particle (VLP) Vaccine Administered to 16- to 26-Year-Old Women

Summary

EudraCT number	2007-003528-39
Trial protocol	DK SE DE AT Outside EU/EEA
Global end of trial date	07 July 2016

Results information

Result version number	v1 (current)
This version publication date	04 January 2017
First version publication date	04 January 2017

Trial information

Trial identification

Sponsor protocol code	V503-001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00543543
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000654-PIP01-09
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the safety, efficacy, and immunogenicity of V503 in comparison to GARDASIL. The primary hypotheses tested in the study were 1) V503 administered to 16- to 26-year-old adolescents and young women is generally well-tolerated, 2) V503 reduces combined incidence of Human Papillomavirus (HPV) Type 31/33/45/52/58-related disease compared with GARDASIL, and 3) V503 induces non-inferior geometric mean titers for HPV Type 6/11/16/18 antibodies compared with GARDASIL.
The study included a dose-finding evaluation of a 3-dose regimen of V503 and GARDASIL, a safety/efficacy evaluation of a 3-dose regimen of the selected V503 dose formulation and GARDASIL, and an extension consisting of 2 substudies: an evaluation of immune memory in participants receiving a fourth vaccination with V503 (Cohort 1), and an opportunity for participants who received GARDASIL in the Base Study to receive a 3-dose regimen of V503 (Cohort 2).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research. The following additional measure(s) defined for this individual study was (were) in place for the protection of trial subjects: participants who received GARDASIL in the Base Study will have the opportunity to receive a 3-dose regimen of V503 in the study extension (Cohort 2).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 168
Country: Number of subjects enrolled	Brazil: 765
Country: Number of subjects enrolled	Canada: 1442
Country: Number of subjects enrolled	Chile: 140
Country: Number of subjects enrolled	Colombia: 2499
Country: Number of subjects enrolled	Denmark: 3731
Country: Number of subjects enrolled	Germany: 194
Country: Number of subjects enrolled	Hong Kong: 160
Country: Number of subjects enrolled	Japan: 254
Country: Number of subjects enrolled	Korea, Republic of: 307
Country: Number of subjects enrolled	New Zealand: 97

Country: Number of subjects enrolled	Norway: 710
Country: Number of subjects enrolled	Peru: 785
Country: Number of subjects enrolled	Puerto Rico: 42
Country: Number of subjects enrolled	Sweden: 128
Country: Number of subjects enrolled	Taiwan: 600
Country: Number of subjects enrolled	Thailand: 465
Country: Number of subjects enrolled	United States: 1572
Country: Number of subjects enrolled	Mexico: 781
Worldwide total number of subjects	14840
EEA total number of subjects	4931

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)	343
Adults (18-64 years)	14497
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study enrolled healthy young women 16 to 26 years of age.

Pre-assignment

Screening details:

A total of 15,334 participants were screened and 14,840 were randomized into the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Low-dose V503

Arm description:

V503 (9-Valent Human Papillomavirus [HPV] Vaccine) low-dose 0.5 mL injection in a 3-dose regimen in the Base Study.

Arm type	Experimental
Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Arm title	Mid-dose V503

Arm description:

V503 mid-dose 0.5 mL injection in a 3-dose regimen in the Base Study. A subset of participants will receive a fourth V503 mid-dose vaccination in the extension study (Cohort 1).

Arm type	Experimental
Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Arm title	High-dose V503

Arm description:

V503 high-dose 0.5 mL injection in a 3-dose regimen in the Base Study

Arm type	Experimental

Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Arm title	Gardasil

Arm description:

Gardasil (4-Valent HPV Vaccine) 0.5 mL injection in a 3-dose regimen in the Base Study. Participants will be offered the V503 mid-dose 3-dose regimen in the extension study (Cohort 2).

Arm type	Active comparator
Investigational medicinal product name	GARDASIL (4-Valent HPV [Types 6, 11, 16, and 18] L1 virus-like particle vaccine)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Number of subjects in period 1	Low-dose V503	Mid-dose V503	High-dose V503
Started	315	7106	310
Completed 3 vaccinations in Base Study	300	6928	297
Completed	295	5854	296
Not completed	20	1252	14
Consent withdrawn by subject	7	482	5
Physician decision	-	4	-
Adverse event, non-fatal	1	11	-
Lost to follow-up	12	749	9
Protocol deviation	-	6	-

Number of subjects in period 1	Gardasil
Started	7109
Completed 3 vaccinations in Base Study	6934
Completed	5887
Not completed	1222
Consent withdrawn by subject	503
Physician decision	7
Adverse event, non-fatal	5
Lost to follow-up	701
Protocol deviation	6

Period 2

Period 2 title	Extension Study
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mid-dose V503 (Cohort 1)

Arm description:

V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL fourth dose administration on Base Study participants who were randomized to receive a 3-dose regimen of V503 (9-Valent HPV) mid-dose 0.5 mL (Cohort 1).

Arm type	Experimental
Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle at Month 60 in the Extension Study

Arm title	Mid-dose V503 (Cohort 2)

Arm description:

V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL 3-dose regimen administration on Base Study participants who were randomized to receive a 3-dose regimen of Gardasil (4-Valent HPV Vaccine) (Cohort 2).

Arm type	Experimental
Investigational medicinal product name	V503 9-valent HPV (Types 6, 11, 16, 18, 31, 33, 45, 52, and 58) L1 virus-like particle vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle at Month 60, 62 and 66 of the Extension Study

Investigational medicinal product name	GARDASIL (4-Valent HPV [Types 6, 11, 16, and 18] L1 virus-like particle vaccine)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL injection in the non-dominant deltoid muscle on Day 1, Month 2 and Month 6 of the Base Study

Number of subjects in period 2[1]	Mid-dose V503 (Cohort 1)	Mid-dose V503 (Cohort 2)
Started	150	3050
Completed	150	2824
Not completed	0	226
Physician decision	-	7
Consent withdrawn by subject	-	120
Adverse event, non-fatal	-	5
Pregnancy	-	6
Lost to follow-up	-	77
Protocol deviation	-	11

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Enrollment in Cohorts 1 and 2 was voluntary; not all eligible participants enrolled in these cohorts.

Baseline characteristics

Reporting groups	
Reporting group title	Low-dose V503
Reporting group description:	
V503 (9-Valent Human Papillomavirus [HPV] Vaccine) low-dose 0.5 mL injection in a 3-dose regimen in the Base Study.	
Reporting group title	Mid-dose V503
Reporting group description:	
V503 mid-dose 0.5 mL injection in a 3-dose regimen in the Base Study. A subset of participants will receive a fourth V503 mid-dose vaccination in the extension study (Cohort 1).	
Reporting group title	High-dose V503
Reporting group description:	
V503 high-dose 0.5 mL injection in a 3-dose regimen in the Base Study	
Reporting group title	Gardasil
Reporting group description:	
Gardasil (4-Valent HPV Vaccine) 0.5 mL injection in a 3-dose regimen in the Base Study. Participants will be offered the V503 mid-dose 3-dose regimen in the extension study (Cohort 2).	

Reporting group values	Low-dose V503	Mid-dose V503	High-dose V503
Number of subjects	315	7106	310
Age Categorical Units: Subjects			
Adolescents (12-17 years)	3	170	3
Adults (18-64 years)	312	6936	307
Age Continuous Units: years			
arithmetic mean	21.7	21.9	21.9
standard deviation	± 2.4	± 2.5	± 2.4
Gender Categorical Units: Subjects			
Female	315	7106	310
Male	0	0	0

Reporting group values	Gardasil	Total	
Number of subjects	7109	14840	
Age Categorical Units: Subjects			
Adolescents (12-17 years)	167	343	
Adults (18-64 years)	6942	14497	
Age Continuous Units: years			
arithmetic mean	21.8		
standard deviation	± 2.5	-	
Gender Categorical Units: Subjects			
Female	7109	14840	
Male	0	0	

End points

End points reporting groups

Reporting group title	Low-dose V503
Reporting group description:	
V503 (9-Valent Human Papillomavirus [HPV] Vaccine) low-dose 0.5 mL injection in a 3-dose regimen in the Base Study.	
Reporting group title	Mid-dose V503
Reporting group description:	
V503 mid-dose 0.5 mL injection in a 3-dose regimen in the Base Study. A subset of participants will receive a fourth V503 mid-dose vaccination in the extension study (Cohort 1).	
Reporting group title	High-dose V503
Reporting group description:	
V503 high-dose 0.5 mL injection in a 3-dose regimen in the Base Study	
Reporting group title	Gardasil
Reporting group description:	
Gardasil (4-Valent HPV Vaccine) 0.5 mL injection in a 3-dose regimen in the Base Study. Participants will be offered the V503 mid-dose 3-dose regimen in the extension study (Cohort 2).	
Reporting group title	Mid-dose V503 (Cohort 1)
Reporting group description:	
V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL fourth dose administration on Base Study participants who were randomized to receive a 3-dose regimen of V503 (9-Valent HPV) mid-dose 0.5 mL (Cohort 1).	
Reporting group title	Mid-dose V503 (Cohort 2)
Reporting group description:	
V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL 3-dose regimen administration on Base Study participants who were randomized to receive a 3-dose regimen of Gardasil (4-Valent HPV Vaccine) (Cohort 2).	

Primary: Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related High-Grade Disease (Test of Hypothesis)

End point title	Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related High-Grade Disease (Test of Hypothesis)[1]
End point description:	
HPV Type 31/33/45/52/58-related high-grade Cervical Intraepithelial Neoplasia (CIN 2/3), Adenocarcinoma in Situ (AIS), Invasive Cervical Carcinoma, high-grade Vulvar Intraepithelial Neoplasia (VIN 2/3), high-grade Vaginal Intraepithelial Neoplasia (VaIN 2/3), vulvar cancer, or vaginal cancer were determined by clinical/pathologic criteria and positive Polymerase Chain Reaction (PCR) assay for virus subtype. This outcome measure reports data based on the protocol-specified plan of conducting hypothesis testing when at least 30 cases had accumulated. Disease incidence was defined as the number of primary efficacy cases per 10,000 person-years of follow-up in a treatment arm. The Per-protocol Efficacy population included all participants who received all 3 vaccinations of mid-dose V503 or Gardasil within acceptable day ranges, were seronegative at Day 1 and PCR negative at Day 1 through Day 7 to the relevant HPV types, and had at least 1 follow-up visit following Month 7.	
End point type	Primary
End point timeframe:	
From Month 7 until >=30 cases accumulate, up to Month 54 in the base study	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint applied only to the Mid-dose V503 and Gardasil groups.

End point values	Mid-dose V503	Gardasil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6016	6017		
Units: Cases per 10,000 person-years follow-up				
number (not applicable)	0.5	15.8		

Statistical analyses

Statistical analysis title	V503 Vaccine Efficacy
Statistical analysis description:	
Vaccine efficacy = 100 * [1 - (incidence rate with V503 / incidence rate with Gardasil)]	
Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	12033
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.0001
Method	Chan and Bohidar Exact Binomial
Parameter estimate	Vaccine Efficacy
Point estimate	96.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	80.9
upper limit	99.8

Notes:

[2] - The pre-specified success criterion was a lower bound of the 95% confidence interval of observed efficacy of >25%

Primary: Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related High-Grade Disease (End-of-study Update)

End point title	Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related High-Grade Disease (End-of-study Update)[3]

End point description:

HPV Type 31/33/45/52/58-related high-grade Cervical Intraepithelial Neoplasia (CIN 2/3), Adenocarcinoma in Situ (AIS), Invasive Cervical Carcinoma, high-grade Vulvar Intraepithelial Neoplasia (VIN 2/3), high-grade Vaginal Intraepithelial Neoplasia (VaIN 2/3), vulvar cancer, or vaginal cancer were determined by clinical/pathologic criteria and positive Polymerase Chain Reaction (PCR) assay for virus subtype. This outcome measure reports cumulative study data through 10 March 2014. Disease incidence was defined as the number of primary efficacy cases per 10,000 person-years of follow-up in a treatment arm. The Per-protocol Efficacy population included all participants who received all 3 vaccinations of mid-dose V503 or Gardasil within acceptable day ranges, were seronegative at Day 1 and PCR negative at Day 1 through Day 7 to the relevant HPV types, and had at least 1 follow-up visit following Month 7.

End point type	Primary

End point timeframe:

From Month 7 up to Month 54 in the Base Study

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint applied only to the mid-dose V503 and Gardasil groups.

End point values	Mid-dose V503	Gardasil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6016	6017		
Units: Cases per 10,000 person-years follow-up				
number (not applicable)	0.5	19		

Statistical analyses

Statistical analysis title	V503 Vaccine Efficacy (End-of-Study Update)
Statistical analysis description:	
Vaccine efficacy = 100 * [1 - (incidence rate with V503 / incidence rate with Gardasil)]	
Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	12033
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Vaccine Efficacy
Point estimate	97.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	85
upper limit	99.9

Notes:

[4] - The pre-specified success criterion was a lower bound of the 95% confidence interval of observed efficacy of >25%

Primary: Base Study: Geometric Mean Titers (GMTs) to HPV Types 6/11/16/18/31/33/45/52/58

End point title	Base Study: Geometric Mean Titers (GMTs) to HPV Types 6/11/16/18/31/33/45/52/58[5]

End point description:

Serum antibodies to HPV types 6/11/16/18/31/33/45/52/58 were measured with a Competitive Luminex Immunoassay. Titers are reported in milli Merck Units/mL. Statistical analysis was performed only for HPV types contained in both vaccines. The Per-protocol Immunogenicity population included all participants who were not protocol violators, received all 3vaccinations of mid-dose V503 or Gardasil within acceptable ranges, were seronegative at Day 1 and PCR negative from Day 1 to Month 7 for the relevant HPV types, and had a Month 7 serum sample collected within an acceptable range. A value of 9999 means less than the limit of quantification. Statistical analysis was performed only for HPV types contained in both vaccines.

End point type	Primary

End point timeframe:

4 weeks postdose 3 in the Base Study

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint applied only to the mid-dose V503 and Gardasil groups.

End point values	Mid-dose V503	Gardasil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6792	6795		
Units: milli Merck U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=3993, 3975)	893.1 (871.7 to 915.1)	875.2 (854.2 to 896.8)		
Anti-HPV Type 11 (n=3995, 3982)	666.3 (649.6 to 683.4)	830 (809.2 to 851.4)		
Anti-HPV Type 16 (n=4032, 4062)	3131.1 (3057.1 to 3206.9)	3156.6 (3082.3 to 3232.7)		
Anti-HPV Type 18 (n=4539, 4541)	804.6 (782.7 to 827.1)	678.7 (660.2 to 697.7)		
Anti-HPV Type 31 (n=4466, 4377)	658.4 (636.7 to 680.9)	9.7 (9.4 to 10.1)		
Anti-HPV Type 33 (n=4702, 4691)	415.9 (405.6 to 426.4)	9999 (9999 to 9999)		
Anti-HPV Type 45 (n=4792, 4750)	252.8 (246.2 to 259.6)	9999 (9999 to 9999)		
Anti-HPV Type 52 (n=4455, 4335)	379.7 (371.6 to 388)	9999 (9999 to 9999)		
Anti-HPV Type 58 (n=4486, 4446)	482.5 (469.9 to 495.3)	9999 (9999 to 9999)		

Statistical analyses

Statistical analysis title	Non-inferiority anti-HPV Type 6
Statistical analysis description:	
Non-inferiority required that the lower bound of the two-sided confidence interval (CI) of the GMT ratio was >0.67	
Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	13587
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio = GMT (V503) / GMT (Gardasil)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.99
upper limit	1.06

Statistical analysis title	Non-inferiority anti-HPV Type 11
Statistical analysis description:	
Non-inferiority required that the lower bound of the two-sided confidence interval (CI) of the GMT ratio was >0.67	
Comparison groups	Mid-dose V503 v Gardasil

Number of subjects included in analysis	13587
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio = GMT (V503) / GMT (Gardasil)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	0.83

Statistical analysis title	Non-inferiority anti-HPV Type 16
Statistical analysis description:	
Non-inferiority required that the lower bound of the two-sided CI of the GMT ratio was >0.67	
Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	13587
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio = GMT (V503) / GMT (Gardasil)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.03

Statistical analysis title	Non-inferiority anti-HPV Type 18
Statistical analysis description:	
Non-inferiority required that the lower bound of the two-sided CI of the GMT ratio was >0.67	
Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	13587
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	GMT ratio = GMT (V503) / GMT (Gardasil)
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.14
upper limit	1.23

Primary: Base Study: Percentage of Participants With One or More Adverse Event

End point title	Base Study: Percentage of Participants With One or More Adverse Event[6]

End point description:

An adverse event (AE) is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. The analysis population included all participants who received >=1 vaccination and had safety follow-up.

End point type	Primary

End point timeframe:

Up to Month 7 (low- and high-dose V503) or up to Month 54 (mid-dose V503 and Gardasil)

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: No statistical analysis was planned for Percentage of Participants With One or More Adverse Event.

End point values	Low-dose V503	Mid-dose V503	High-dose V503	Gardasil
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	7071	305	7078
Units: Percentage of participants				
number (not applicable)	92.6	94.2	92.8	91.1

Statistical analyses

No statistical analyses for this end point

Primary: Base Study: Percentage of Participants With One or More Injection-site Adverse Event

End point title	Base Study: Percentage of Participants With One or More Injection-site Adverse Event[7]

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. AEs such as redness, swelling, and pain/tenderness/soreness at the injection site were recorded. The analysis population included all participants who received >=1 vaccination and had safety follow-up.

End point type	Primary

End point timeframe:

Up to Day 5 after any vaccination in the Base Study

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: No statistical analysis was planned for Percentage of Participants With One or More Injection-site Adverse Event.

End point values	Low-dose V503	Mid-dose V503	High-dose V503	Gardasil
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	7071	305	7078
Units: Percentage of participants				
number (not applicable)	87.7	90.7	90.5	84.9

Statistical analyses

No statistical analyses for this end point

Primary: Base Study: Percentage of Participants With One or More Non-injection-site (Systemic) Adverse Event

End point title	Base Study: Percentage of Participants With One or More Non-injection-site (Systemic) Adverse Event[8]

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. Systemic AEs were those not categorized as injection-site AEs. The analysis population included all participants who received >=1 vaccination and had safety follow-up.

End point type	Primary

End point timeframe:

Up to Day 15 after any vaccination in the Base Study

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: No statistical analysis was planned for Percentage of Participants With One or More Non-injection-site (Systemic) Adverse Event.

End point values	Low-dose V503	Mid-dose V503	High-dose V503	Gardasil
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	7071	305	7078
Units: Percentage of participants				
number (not applicable)	53.5	55.8	51.1	54.9

Statistical analyses

No statistical analyses for this end point

Primary: Base Study: Percentage of Participants With One or More Vaccine-related Adverse Event

End point title	Base Study: Percentage of Participants With One or More Vaccine-related Adverse Event[9]

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an adverse event. An AE that is judged by the investigator to be "definitely related," "probably related," or "possibly related" to the study drug is defined as a vaccine-related AE. The analysis population included all participants who received >=1 vaccination and had

safety follow-up.

End point type	Primary

End point timeframe:

Up to Month 7 (low- and high-dose V503) or up to Month 54 (mid-dose V503 and Gardasil)

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: No statistical analysis was planned for Percentage of Participants With One or More Vaccine-related Adverse Event.

End point values	Low-dose V503	Mid-dose V503	High-dose V503	Gardasil
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	7071	305	7078
Units: Percentage of participants				
number (not applicable)	90	92.2	92.8	87.6

Statistical analyses

No statistical analyses for this end point

Primary: Base Study: Percentage of Participants With Study Medication Withdrawn Due to an Adverse Event

End point title	Base Study: Percentage of Participants With Study Medication Withdrawn Due to an Adverse Event[10]

End point description:

An AE is defined as any unfavorable and unintended change in the structure, function, or chemistry of the body temporally associated with the use of the study vaccine, whether or not considered related to the use of the product. Any worsening of a preexisting condition which is temporally associated with the use of the study vaccine is also an AE. The analysis population included all participants who received >=1 vaccination and had safety follow-up.

End point type	Primary

End point timeframe:

Up to Month 6

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: No statistical analysis was planned for Percentage of Participants With Study Medication Withdrawn Due to an Adverse Event.

End point values	Low-dose V503	Mid-dose V503	High-dose V503	Gardasil
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	310	7071	305	7078
Units: Percentage of participants				
number (not applicable)	0.6	0.1	0	0.1

Statistical analyses

No statistical analyses for this end point

Primary: Extension Study (Immune Memory Substudy): Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Day 7 Postdose 4

End point title	Extension Study (Immune Memory Substudy): Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Day 7 Postdose 4[11]

End point description:

Serum antibodies to HPV types 6/11/16/18/31/33/45/52/58 were measured with a Competitive Luminex Immunoassay. Titers are reported in milli Merck Units/mL. The Per-Protocol Immunogenicity population (Cohort 1) included all participants who were not protocol violators, received all 3 vaccinations of mid-dose V503 in the Base Study and a fourth dose in the Extension Study within acceptable ranges, were seronegative at Day 1 and PCR negative from Day 1 to Month7 for the relevant HPV types, and had a Month 60 serum sample collected within an acceptable range.

End point type	Primary

End point timeframe:

Month 60 + 1 week: Day 7 postdose 4 in the Extension Study (Cohort 1)

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: No statistical analysis was planned for Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Day 7 Postdose 4.

End point values	Mid-dose V503 (Cohort 1)			
Subject group type	Reporting group			
Number of subjects analysed	150			
Units: milli Merck U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=109)	2180.5 (1826.2 to 2603.7)			
Anti-HPV Type 11 (n=109)	2228.7 (1852.5 to 2681.3)			
Anti-HPV Type 16 (n=126)	7986.3 (6795.7 to 9385.6)			
Anti-HPV Type 18 (n=138)	2399 (2049.4 to 2808.1)			
Anti-HPV Type 31 (n=131)	1462.2 (1263.9 to 1691.5)			
Anti-HPV Type 33 (n=137)	1709 (1466.7 to 1991.2)			
Anti-HPV Type 45 (n=144)	323 (277.2 to 376.5)			
Anti-HPV Type 52 (n=131)	1078.1 (907.2 to 1281.2)			
Anti-HPV Type 58 (n=129)	1801.8 (1530.5 to 2121.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Extension Study (Immune Memory Substudy): Geometric Mean Titers to

HPV Types 6/11/16/18/31/33/45/52/58 at Day 28 Postdose 4

End point title	Extension Study (Immune Memory Substudy): Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Day 28 Postdose 4[12]

End point description:

Serum antibodies to HPV types 6/11/16/18/31/33/45/52/58 were measured with a Competitive Luminex Immunoassay. Titers are reported in milli Merck Units/mL. The Per-Protocol Immunogenicity population (Cohort 1) included all participants who were not protocol violators, received all 3 vaccinations of mid-dose V503 in the Base Study and a fourth dose in the Extension Study within acceptable ranges, were seronegative at Day 1 and PCR negative from Day 1 to Month7 for the relevant HPV types, and had a Month 60 serum sample collected within an acceptable range.

End point type	Primary

End point timeframe:

Month 61: 28 days postdose 4 in the Extension Study (Cohort 1)

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: No statistical analysis was planned for Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Day 28 Postdose 4.

End point values	Mid-dose V503 (Cohort 1)			
Subject group type	Reporting group			
Number of subjects analysed	150			
Units: milli Merck U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=109)	2585 (2239.5 to 2983.8)			
Anti-HPV Type 11 (n=109)	2548.7 (2191.4 to 2964.3)			
Anti-HPV Type 16 (n=123)	10904.3 (9605.6 to 12378.7)			
Anti-HPV Type 18 (n=137)	2907.9 (2531.1 to 3340.7)			
Anti-HPV Type 31 (n=130)	1745.4 (1538.8 to 1979.8)			
Anti-HPV Type 33 (n=136)	2094.9 (1848.7 to 2373.9)			
Anti-HPV Type 45 (n=143)	440 (386.9 to 500.4)			
Anti-HPV Type 52 (n=129)	1131.5 (991.6 to 1291.1)			
Anti-HPV Type 58 (n=127)	2024.6 (1803.1 to 2273.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related

Persistent Infection

End point title	Base Study: Combined Incidence of HPV Type 31/33/45/52/58-related Persistent Infection[13]

End point description:

Combined Incidence of HPV Type 31/33/45/52/58-related persistent infection as determined by clinical/pathologic criteria and positive Polymerase Chain Reaction (PCR) assay for virus subtype. Persistent infection was defined as infection detected in samples from >=2 consecutive visits 6 months (+/-1 month visit window) or longer apart. Incidence was defined as the number of cases of persistent infection per 10,000 person-years of follow-up in a treatment arm. The Per-protocol Efficacy population included all participants who received all 3 vaccinations of mid-dose V503 or Gardasil within acceptable day ranges, were seronegative at Day 1 and PCR negative at Day 1 through Day 7 to the relevant HPV types, and had at least 1 follow-up visit following Month 7.

End point type	Secondary

End point timeframe:

Up to Month 54 in the Base Study

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint applied only to the mid-dose V503 and Gardasil groups.

End point values	Mid-dose V503	Gardasil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5941	5955		
Units: Cases per 10,000 person-years follow-up				
number (not applicable)	21.5	538.8		

Statistical analyses

Statistical analysis title	Vaccine Efficacy

Statistical analysis description:

Vaccine efficacy = 100 * [1 - (incidence rate with V503 / incidence rate with Gardasil)]

Comparison groups	Mid-dose V503 v Gardasil
Number of subjects included in analysis	11896
Analysis specification	Pre-specified
Analysis type	other[14]
Parameter estimate	Vaccine Efficacy
Point estimate	96
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.6
upper limit	97.1

Notes:

[14] - The pre-specified success criterion was a lower bound of the 95% confidence interval of observed efficacy of >25%

Secondary: Base Study: Percentage of Participants Who Are Seropositive for HPV Types 6/11/16/18/31/33/45/52/58

End point title	Base Study: Percentage of Participants Who Are Seropositive for HPV Types 6/11/16/18/31/33/45/52/58[15]

End point description:

Serum antibodies to HPV types were measured with a Competitive Luminex Immunoassay. The serostatus cutoffs (milli Merck U/mL) for HPV types were as follows: HPV Type 6: ≥30; HPV Type 11: ≥16; HPV Type 16: ≥20; HPV Type 18: ≥24; HPV Type 31: ≥10; HPV Types 33, 45, 52, and 58: ≥8. The Per-protocol Immunogenicity population included all participants who were not protocol violators, received all 3 vaccinations of mid-dose V503 or Gardasil within acceptable ranges, were seronegative at Day 1 and PCR negative from Day 1 - Month 7 for the relevant HPV types, and had a Month 7 serum sample collected within an acceptable range.

End point type	Secondary

End point timeframe:

4 weeks postdose 3 in the Base Study

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint applied only to the mid-dose V503 and Gardasil groups.

End point values	Mid-dose V503	Gardasil		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6792	6795		
Units: Percentage of participants				
number (confidence interval 95%)				
Anti-HPV Type 6 (n=3993, 3975)	99.8 (99.6 to 99.9)	99.8 (99.7 to 99.9)		
Anti-HPV Type 11 (n=3995, 3982)	100 (99.9 to 100)	99.9 (99.8 to 100)		
Anti-HPV Type 16 (n=4032, 4062)	100 (99.9 to 100)	100 (99.9 to 100)		
Anti-HPV Type 18 (n=4539, 4541)	99.9 (99.7 to 99.9)	99.7 (99.5 to 99.8)		
Anti-HPV Type 31 (n=4466, 4377)	99.8 (99.6 to 99.9)	50.1 (48.7 to 51.6)		
Anti-HPV Type 33 (n=4702, 4691)	99.7 (99.5 to 99.9)	12.7 (11.8 to 13.7)		
Anti-HPV Type 45 (n=4792, 4750)	99.6 (99.4 to 99.8)	9.2 (8.4 to 10)		
Anti-HPV Type 52 (n=4455, 4335)	99.8 (99.6 to 99.9)	2.6 (2.2 to 3.1)		
Anti-HPV Type 58 (n=4486, 4446)	99.8 (99.6 to 99.9)	20.4 (19.2 to 21.6)		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Extension Study (Immune Memory Substudy): Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Predose 4

End point title	Extension Study (Immune Memory Substudy): Geometric Mean Titers to HPV Types 6/11/16/18/31/33/45/52/58 at Predose 4

End point description:

Serum antibodies to HPV types 6/11/16/18/31/33/45/52/58 were measured with a Competitive Luminex Immunoassay. Titers are reported in milli Merck Units/mL. The Per-Protocol Immunogenicity population (Cohort 1) included all participants who were not protocol violators, received all 3 vaccinations of mid-dose V503 in the Base Study and a fourth dose in the Extension Study within acceptable ranges, were seronegative at Day 1 and PCR negative from Day 1 to Month7 for the relevant HPV types, and had a Month 60 serum sample collected within an acceptable range.

End point type	Other pre-specified

End point timeframe:

Month 60: predose 4 in the Extension Study (Cohort 1)

End point values	Mid-dose V503 (Cohort 1)			
Subject group type	Reporting group			
Number of subjects analysed	150			
Units: milli Merck U/mL				
geometric mean (confidence interval 95%)				
Anti-HPV Type 6 (n=101)	143.1 (117.9 to 173.7)			
Anti-HPV Type 11 (n=112)	82.9 (68.1 to 100.9)			
Anti-HPV Type 16 (n=128)	324.4 (266.7 to 394.7)			
Anti-HPV Type 18 (n=142)	62.5 (49.5 to 78.9)			
Anti-HPV Type 31 (n=135)	69.2 (56.6 to 84.4)			
Anti-HPV Type 33 (n=141)	44.7 (37 to 54.1)			
Anti-HPV Type 45 (n=148)	20.8 (17 to 25.5)			
Anti-HPV Type 52 (n=134)	33.7 (27.6 to 41.1)			
Anti-HPV Type 58 (n=132)	50.9 (40.9 to 63.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Base Study: SAEs up to Month (M) 7 (low- and high-dose V503) or up to M54 (mid-dose V503 and Gardasil); non-serious AEs up to Day 15 after vaccination. Cohort 1: SAEs M60 to 61; non-serious AEs up to Day 15 after vaccination 4. Cohort 2: SAEs M60 to 67.

Adverse event reporting additional description:

The analysis population included all participants who received >=1 vaccination and had safety follow-up.

Non-serious AEs were not solicited in Extension Cohort 2; however, some non-serious AEs were voluntarily reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Base Study: Low-dose V503

Reporting group description:

V503 (9-Valent HPV Vaccine) low-dose 0.5 mL injection in a 3-dose regimen in the Base Study.

Reporting group title	Base Study: Mid-dose V503

Reporting group description:

V503 mid-dose 0.5 mL injection in a 3-dose regimen in the Base Study.

Reporting group title	Base Study: High-dose V503

Reporting group description:

V503 high-dose 0.5 mL injection in a 3-dose regimen in the Base Study.

Reporting group title	Base Study: Gardasil

Reporting group description:

Gardasil (4-Valent HPV Vaccine) 0.5 mL injection in a 3-dose regimen in the Base Study. Participants will be offered the V503 mid-dose 3-dose regimen in the extension study (Cohort 2).

Reporting group title	Extension Study: Mid-dose V503 (Cohort 1)

Reporting group description:

V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL fourth dose administration on Base Study participants who were randomized to receive a 3-dose regimen of V503 (9-Valent HPV) mid-dose 0.5 mL (Cohort 1).

Reporting group title	Extension Study: Mid-dose V503 (Cohort 2)

Reporting group description:

V503 (9-Valent HPV Vaccine) mid-dose 0.5 mL 3-dose regimen administration on Base Study participants who were randomized to receive a 3-dose regimen of Gardasil (4-Valent HPV Vaccine) (Cohort 2).

Serious adverse events	Base Study: Low-dose V503	Base Study: Mid-dose V503	Base Study: High-dose V503
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 310 (1.29%)	233 / 7071 (3.30%)	5 / 305 (1.64%)
number of deaths (all causes)	0	6	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Brain neoplasm			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Ependymoma			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Leukaemic infiltration brain			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Malignant melanoma			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Malignant palate neoplasm			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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 cavity cancer			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Ovarian neoplasm			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Pituitary tumour benign			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Respiratory papilloma			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Thyroid cancer			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Breast cancer			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Glioma			

subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Vascular disorders			
Axillary vein thrombosis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	1 / 310 (0.32%)	73 / 7071 (1.03%)	2 / 305 (0.66%)
occurrences causally related to treatment / all	0 / 1	0 / 76	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 310 (0.32%)	36 / 7071 (0.51%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 1	0 / 38	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous complete			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Abortion spontaneous incomplete			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Blighted ovum			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cephalo-pelvic disproportion			
subjects affected / exposed	0 / 310 (0.00%)	4 / 7071 (0.06%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix dystocia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Ectopic pregnancy			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
False labour			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Foetal death			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal distress syndrome			
subjects affected / exposed	1 / 310 (0.32%)	4 / 7071 (0.06%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal malposition			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Foetal malpresentation			

subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Gestational diabetes			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Labour complication			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Oligohydramnios			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pre-eclampsia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature labour			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Premature rupture of membranes			
subjects affected / exposed	0 / 310 (0.00%)	4 / 7071 (0.06%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged labour			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine contractions during pregnancy			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pyrexia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Immune system disorders			
Allergy to vaccine			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Hypersensitivity			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Sarcoidosis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Reproductive system and breast disorders			
Bartholinitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cervical dysplasia			
subjects affected / exposed	0 / 310 (0.00%)	5 / 7071 (0.07%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Dysmenorrhoea			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Endometriosis			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fallopian tube cyst			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Pelvic pain			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Dyspnoea			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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 polyps			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Pneumothorax			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Respiratory failure			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Vocal cord polyp			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Psychiatric disorders			
Anorexia and bulimia syndrome			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Anorexia nervosa			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Bipolar disorder			
subjects affected / exposed	0 / 310 (0.00%)	3 / 7071 (0.04%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Completed suicide			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Depression			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Major depression			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Bladder injury			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Burns second degree			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Craniocerebral injury			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Femur fracture			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Foreign body in eye			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Fracture displacement			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Hand fracture			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Head injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Humerus fracture			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Ligament rupture			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Lower limb fracture			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Multiple injuries			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Poisoning			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Post procedural haemorrhage			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pubis fracture			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Road traffic accident			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Spinal cord injury			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Spinal cord injury cervical			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Ulna fracture			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Congenital, familial and genetic disorders			
Cleft lip and palate			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Diverticulitis Meckel's			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrial fibrillation			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Benign intracranial hypertension			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Cerebral haemorrhage			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Diabetic coma			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Epilepsy			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Facial paresis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Headache			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Hydrocephalus			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Hypersomnia			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoaesthesia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Migraine			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Multiple sclerosis			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuritis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Orthostatic intolerance			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Presyncope			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Sciatica			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Sensory disturbance			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Spondylitic myelopathy			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Syncope			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tension headache			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Trigeminal nerve disorder			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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			

Abdominal pain			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Abdominal pain lower			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Anal fistula			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Coeliac disease			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Colitis ulcerative			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Crohn's disease			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Diarrhoea			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Enterocolitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Gastritis			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Haemorrhoids			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Inguinal hernia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Omental infarction			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pancreatitis acute			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cholecystitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cholelithiasis			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cholestasis of pregnancy			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Calculus urinary			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Cystitis haemorrhagic			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Nephrolithiasis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Renal failure			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure acute			

subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Renal colic			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Myalgia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Osteoarthritis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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			
Abscess jaw			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Appendicitis			
subjects affected / exposed	1 / 310 (0.32%)	9 / 7071 (0.13%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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

Cellulitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Cholecystitis infective			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Conjunctivitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Dengue fever			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Enteritis infectious			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Haemorrhagic fever			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Influenza			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Pelvic inflammatory disease			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pharyngitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Post abortion infection			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Pyelonephritis			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Septic shock			

subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Tonsillitis streptococcal			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Urinary tract infection			
subjects affected / exposed	0 / 310 (0.00%)	2 / 7071 (0.03%)	1 / 305 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Viral pharyngitis			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Wound infection			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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
Pneumonia			
subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Postoperative wound infection			

subjects affected / exposed	0 / 310 (0.00%)	0 / 7071 (0.00%)	0 / 305 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 310 (0.00%)	1 / 7071 (0.01%)	0 / 305 (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

Serious adverse events	Base Study: Gardasil	Extension Study: Mid-dose V503 (Cohort 1)	Extension Study: Mid-dose V503 (Cohort 2)
Total subjects affected by serious adverse events			
subjects affected / exposed	184 / 7078 (2.60%)	1 / 150 (0.67%)	25 / 3049 (0.82%)
number of deaths (all causes)	5	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Acute promyelocytic leukaemia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Adenocarcinoma gastric			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Adenocarcinoma of the cervix			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain neoplasm			

subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Ependymoma			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Leukaemic infiltration brain			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Malignant melanoma			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Malignant melanoma in situ			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Malignant palate neoplasm			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Nasal cavity cancer			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian neoplasm			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Pituitary tumour benign			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Respiratory papilloma			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Thyroid cancer			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Breast cancer			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioma			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Axillary vein thrombosis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Hypovolaemic shock			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Surgical and medical procedures			

Abortion induced			
subjects affected / exposed	53 / 7078 (0.75%)	0 / 150 (0.00%)	3 / 3049 (0.10%)
occurrences causally related to treatment / all	0 / 53	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	26 / 7078 (0.37%)	0 / 150 (0.00%)	8 / 3049 (0.26%)
occurrences causally related to treatment / all	0 / 28	0 / 0	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous complete			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous incomplete			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Blighted ovum			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Cephalo-pelvic disproportion			
subjects affected / exposed	6 / 7078 (0.08%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix dystocia			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Ectopic pregnancy			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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

False labour			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Foetal death			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Foetal distress syndrome			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Foetal malposition			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Foetal malpresentation			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Gestational diabetes			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labour complication			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Oligohydramnios			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pre-eclampsia			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Premature labour			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Premature rupture of membranes			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prolonged labour			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Uterine contractions during pregnancy			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pyrexia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Sudden death			

subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Immune system disorders			
Allergy to vaccine			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Anaphylactic reaction			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Hypersensitivity			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Sarcoidosis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Reproductive system and breast disorders			
Bartholinitis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Cervical dysplasia			
subjects affected / exposed	3 / 7078 (0.04%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix haemorrhage uterine			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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

Dysmenorrhoea			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Endometriosis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Fallopian tube cyst			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Ovarian cyst			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic pain			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Dyspnoea			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Nasal polyps			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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

Pneumonia aspiration			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Pneumothorax			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Respiratory failure			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Vocal cord polyp			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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			
Anorexia and bulimia syndrome			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Anorexia nervosa			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Bipolar disorder			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Completed suicide			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Depression			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Major depression			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Bladder injury			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Burns second degree			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Craniocerebral injury			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Femur fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body in eye			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Fracture displacement			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Hand fracture			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Head injury			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Humerus fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Joint dislocation			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Lower limb fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Multiple injuries			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Neck injury			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Poisoning			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Post procedural haemorrhage			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Road traffic accident			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Spinal compression fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Spinal cord injury			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Spinal cord injury cervical			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Cleft lip and palate			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Diverticulitis Meckel's			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Postural orthostatic tachycardia syndrome			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Atrial fibrillation			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Benign intracranial hypertension			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Diabetic coma			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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

Epilepsy			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Facial paresis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Headache			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Hypersomnia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Hypoaesthesia			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Migraine			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Multiple sclerosis			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuritis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Orthostatic intolerance			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Sciatica			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Sensory disturbance			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Spondylitic myelopathy			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Syncope			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Tension headache			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Trigeminal nerve disorder			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Anal fistula			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Coeliac disease			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Crohn's disease			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Diarrhoea			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Enterocolitis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Gastritis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Haemorrhoids			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Inguinal hernia			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Irritable bowel syndrome			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Omental infarction			

subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pancreatitis acute			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Cholecystitis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Cholelithiasis			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholestasis of pregnancy			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus ureteric			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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

Calculus urinary			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Cystitis haemorrhagic			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Nephrolithiasis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Renal failure			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Renal failure acute			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Renal colic			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fibromyalgia			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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

Osteoarthritis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess jaw			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Appendicitis			
subjects affected / exposed	16 / 7078 (0.23%)	0 / 150 (0.00%)	2 / 3049 (0.07%)
occurrences causally related to treatment / all	0 / 16	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Cholecystitis infective			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Chronic tonsillitis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Conjunctivitis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Dengue fever			

subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Enteritis infectious			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Gastroenteritis			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Haemorrhagic fever			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Influenza			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pelvic inflammatory disease			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pharyngitis			

subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Post abortion infection			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pyelonephritis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Pyelonephritis acute			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Tonsillitis			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Tonsillitis streptococcal			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Urinary tract infection			
subjects affected / exposed	2 / 7078 (0.03%)	0 / 150 (0.00%)	0 / 3049 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			

subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Viral pharyngitis			
subjects affected / exposed	1 / 7078 (0.01%)	0 / 150 (0.00%)	0 / 3049 (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
Wound infection			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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
Pneumonia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	1 / 3049 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 7078 (0.00%)	1 / 150 (0.67%)	0 / 3049 (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
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 7078 (0.00%)	0 / 150 (0.00%)	0 / 3049 (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

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

Non-serious adverse events	Base Study: Low-dose V503	Base Study: Mid-dose V503	Base Study: High-dose V503
Total subjects affected by non-serious adverse events			
subjects affected / exposed	278 / 310 (89.68%)	6551 / 7071 (92.65%)	280 / 305 (91.80%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	17 / 310 (5.48%)	346 / 7071 (4.89%)	11 / 305 (3.61%)
occurrences (all)	20	405	13

Headache			
subjects affected / exposed	65 / 310 (20.97%)	1879 / 7071 (26.57%)	66 / 305 (21.64%)
occurrences (all)	100	3071	106
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	100 / 310 (32.26%)	2411 / 7071 (34.10%)	91 / 305 (29.84%)
occurrences (all)	157	3597	140
Injection site pain			
subjects affected / exposed	267 / 310 (86.13%)	6360 / 7071 (89.94%)	273 / 305 (89.51%)
occurrences (all)	684	15383	672
Injection site pruritus			
subjects affected / exposed	18 / 310 (5.81%)	389 / 7071 (5.50%)	14 / 305 (4.59%)
occurrences (all)	21	494	16
Injection site swelling			
subjects affected / exposed	100 / 310 (32.26%)	2836 / 7071 (40.11%)	103 / 305 (33.77%)
occurrences (all)	154	4527	168
Pyrexia			
subjects affected / exposed	30 / 310 (9.68%)	469 / 7071 (6.63%)	17 / 305 (5.57%)
occurrences (all)	35	563	19
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	22 / 310 (7.10%)	513 / 7071 (7.25%)	18 / 305 (5.90%)
occurrences (all)	23	617	20
Infections and infestations			
Influenza			
subjects affected / exposed	20 / 310 (6.45%)	312 / 7071 (4.41%)	12 / 305 (3.93%)
occurrences (all)	22	343	12
Nasopharyngitis			
subjects affected / exposed	10 / 310 (3.23%)	376 / 7071 (5.32%)	12 / 305 (3.93%)
occurrences (all)	11	412	13

Non-serious adverse events	Base Study: Gardasil	Extension Study: Mid-dose V503 (Cohort 1)	Extension Study: Mid-dose V503 (Cohort 2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6268 / 7078 (88.56%)	130 / 150 (86.67%)	89 / 3049 (2.92%)

Nervous system disorders			
Dizziness			
subjects affected / exposed	307 / 7078 (4.34%)	0 / 150 (0.00%)	2 / 3049 (0.07%)
occurrences (all)	368	0	2
Headache			
subjects affected / exposed	1756 / 7078 (24.81%)	32 / 150 (21.33%)	11 / 3049 (0.36%)
occurrences (all)	2788	41	13
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	1810 / 7078 (25.57%)	33 / 150 (22.00%)	9 / 3049 (0.30%)
occurrences (all)	2564	34	9
Injection site pain			
subjects affected / exposed	5911 / 7078 (83.51%)	124 / 150 (82.67%)	59 / 3049 (1.94%)
occurrences (all)	13001	128	94
Injection site pruritus			
subjects affected / exposed	282 / 7078 (3.98%)	1 / 150 (0.67%)	1 / 3049 (0.03%)
occurrences (all)	341	1	1
Injection site swelling			
subjects affected / exposed	2035 / 7078 (28.75%)	49 / 150 (32.67%)	12 / 3049 (0.39%)
occurrences (all)	2988	51	12
Pyrexia			
subjects affected / exposed	463 / 7078 (6.54%)	6 / 150 (4.00%)	7 / 3049 (0.23%)
occurrences (all)	550	6	7
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	459 / 7078 (6.48%)	2 / 150 (1.33%)	4 / 3049 (0.13%)
occurrences (all)	551	2	4
Infections and infestations			
Influenza			
subjects affected / exposed	296 / 7078 (4.18%)	4 / 150 (2.67%)	5 / 3049 (0.16%)
occurrences (all)	314	5	5
Nasopharyngitis			
subjects affected / exposed	389 / 7078 (5.50%)	1 / 150 (0.67%)	0 / 3049 (0.00%)
occurrences (all)	420	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 November 2008	Amendment 1: Revised the primary objective and hypothesis for measuring efficacy of the V503 vaccine against infection and disease caused by HPV Types 31, 33, 45, 52, and 58.
18 August 2011	Amendment 2: Updated the data analysis related to the secondary objective pertaining to reduction in combined incidence of HPV Types 31, 33, 45, 52, and 58-related persistent infection. Specifically, the statistical criterion for success relating to the lower bound of the 95% confidence interval was changed from 0% to 25%.
04 May 2012	Amendment 3: Added two study visits, Month 48 and Month 54, to help ensure that an adequate number of primary efficacy endpoints were accrued to perform the primary efficacy analysis before the study ended.
14 October 2013	Amendment 4: Added an extension to the V503-001 Base Study, with the goals to 1) assess whether immunogenicity of a fourth dose of V503 vaccine shows evidence of immune memory, and 2) to offer a 3-dose regimen of V503 vaccine to participants in the control arm of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported