



Clinical trial results:

A Phase IIA, open-label study to evaluate the immunogenicity and safety of sequential use of GSK's investigational vaccine GSK3277511A when administered to healthy smokers and ex-smokers aged 50 to 80 years following receipt of Shingrix vaccine

Summary

EudraCT number	2018-002977-24
Trial protocol	ES FI FR IT
Global end of trial date	31 August 2020

Results information

Result version number	v1
This version publication date	22 September 2021
First version publication date	22 September 2021

Trial information

Trial identification

Sponsor protocol code	209538
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03894969
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	GSK Response Center, GSKClinicalSupportHD@gsk.com, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 August 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 August 2020
Global end of trial reached?	Yes
Global end of trial date	31 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority (NI) of the humoral immune response 1 month after Dose 2 of GSK's Non-Typeable Haemophilus influenzae (NTHi) and Moraxella catarrhalis (Mcat) vaccine adjuvanted with AS01E, when administered after vaccination with the AS01B-adjuvanted Shingrix vaccine.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of the vaccines, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Estonia: 193
Country: Number of subjects enrolled	Finland: 156
Country: Number of subjects enrolled	France: 60
Country: Number of subjects enrolled	Italy: 66
Country: Number of subjects enrolled	Spain: 66
Worldwide total number of subjects	541
EEA total number of subjects	541

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	396

From 65 to 84 years	145
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

542 participants were enrolled in the study, but only 541 received at least 1 dose of study treatment (i.e. Shingrix and/or NTHi Mcat vaccine).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sh_NTHi-Mcat_1 Group

Arm description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, and following a 1-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 91, and Day 151.

Arm type	Experimental
Investigational medicinal product name	Shingrix, NTHi-Mcat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of GSK's Shingrix vaccine at Day 1, Day 61 and, following a 1-month gap, 2 doses of GSK Biological's NTHi-Mcat investigational vaccine at Day 91, and Day 151.

Arm title	Sh_NTHi-Mcat_3 Group
------------------	----------------------

Arm description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 3-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 151 and Day 211.

Arm type	Experimental
Investigational medicinal product name	Shingrix, NTHi-Mcat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of GSK's Shingrix vaccine at Day 1, Day 61 and, following a 3-month gap, 2 doses of GSK Biological's NTHi-Mcat investigational vaccine at Day 151 and Day 211.

Arm title	Sh_NTHi-Mcat_6 Group
------------------	----------------------

Arm description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 6-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart at Day 241 and Day 301.

Arm type	Experimental
----------	--------------

Investigational medicinal product name	Shingrix, NTHi-Mcat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of GSK's Shingrix vaccine at Day 1, Day 61 and, following a 6-month gap, 2 doses of GSK Biological's NTHi-Mcat investigational vaccine at Day 241 and Day 301.

Arm title	NTHi-Mcat Group
------------------	-----------------

Arm description:

Subjects enrolled in this group received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 1 and Day 61.

Arm type	Active comparator
Investigational medicinal product name	NTHi-Mcat investigational vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 2 doses of GSK's NTHi-Mcat investigational vaccine at Day 1 and Day 61.

Arm title	Shingrix-Only Group
------------------	---------------------

Arm description:

Subjects belonging to this group were originally randomized to either Sh_NTHi-Mcat_1 Group, Sh_NTHi-Mcat_3 Group or Sh_NTHi-Mcat_6 Group, they received at least 1, maximum 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, but didn't receive any dose of NTHi Mcat investigational vaccine. Only safety data were collected for these subjects.

Arm type	Experimental
Investigational medicinal product name	Shingrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received at least 1, maximum 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61.

Number of subjects in period 1	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group
Started	134	134	122
Completed	132	131	120
Not completed	2	3	2
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	-	2	-
Not specified	-	-	-
Lost to follow-up	1	-	1

Number of subjects in period 1	NTHi-Mcat Group	Shingrix-Only Group
Started	135	16

Completed	129	2
Not completed	6	14
Consent withdrawn by subject	3	8
Adverse event, non-fatal	3	3
Not specified	-	3
Lost to follow-up	-	-

Baseline characteristics

Reporting groups

Reporting group title	Sh_NTHi-Mcat_1 Group
Reporting group description:	
Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, and following a 1-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 91, and Day 151.	
Reporting group title	Sh_NTHi-Mcat_3 Group
Reporting group description:	
Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 3-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 151 and Day 211.	
Reporting group title	Sh_NTHi-Mcat_6 Group
Reporting group description:	
Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 6-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart at Day 241 and Day 301.	
Reporting group title	NTHi-Mcat Group
Reporting group description:	
Subjects enrolled in this group received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 1 and Day 61.	
Reporting group title	Shingrix-Only Group
Reporting group description:	
Subjects belonging to this group were originally randomized to either Sh_NTHi-Mcat_1 Group, Sh_NTHi-Mcat_3 Group or Sh_NTHi-Mcat_6 Group, they received at least 1, maximum 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, but didn't receive any dose of NTHi Mcat investigational vaccine. Only safety data were collected for these subjects.	

Reporting group values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group
Number of subjects	134	134	122
Age categorical			
Units: Subjects			
Adults (18-64 years)	95	103	82
From 65-84 years	39	31	40
Age Continuous			
Units: Years			
arithmetic mean	60.7	60.9	60.5
standard deviation	± 7.0	± 6.7	± 7.1
Sex: Female, Male			
Units: Participants			
Female	63	66	58
Male	71	68	64
Race/Ethnicity, Customized			
Units: Subjects			
American Indian Or Alaska Native	1	0	0
Black Or African American	0	1	0
Not Reported	0	0	0
Other	4	3	2
White	129	130	120

Reporting group values	NTHi-Mcat Group	Shingrix-Only Group	Total
Number of subjects	135	16	541
Age categorical Units: Subjects			
Adults (18-64 years)	104	12	396
From 65-84 years	31	4	145
Age Continuous Units: Years			
arithmetic mean	60.0	62.4	
standard deviation	± 7.1	± 5.5	-
Sex: Female, Male Units: Participants			
Female	65	7	259
Male	70	9	282
Race/Ethnicity, Customized Units: Subjects			
American Indian Or Alaska Native	1	0	2
Black Or African American	1	0	2
Not Reported	0	1	1
Other	4	4	17
White	129	11	519

End points

End points reporting groups

Reporting group title	Sh_NTHi-Mcat_1 Group
Reporting group description: Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, and following a 1-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 91, and Day 151.	
Reporting group title	Sh_NTHi-Mcat_3 Group
Reporting group description: Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 3-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 151 and Day 211.	
Reporting group title	Sh_NTHi-Mcat_6 Group
Reporting group description: Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 6-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart at Day 241 and Day 301.	
Reporting group title	NTHi-Mcat Group
Reporting group description: Subjects enrolled in this group received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 1 and Day 61.	
Reporting group title	Shingrix-Only Group
Reporting group description: Subjects belonging to this group were originally randomized to either Sh_NTHi-Mcat_1 Group, Sh_NTHi-Mcat_3 Group or Sh_NTHi-Mcat_6 Group, they received at least 1, maximum 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, but didn't receive any dose of NTHi Mcat investigational vaccine. Only safety data were collected for these subjects.	

Primary: Anti-Protein D (PD), Anti-Protein E (PE), Anti-type IV pili subunit (PilA) and Anti-ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) Adjusted Geometric Mean Concentrations (GMCs), one-month post Dose-2 of NTHi-Mcat vaccine

End point title	Anti-Protein D (PD), Anti-Protein E (PE), Anti-type IV pili subunit (PilA) and Anti-ubiquitous surface protein A2 of Moraxella catarrhalis (UspA2) Adjusted Geometric Mean Concentrations (GMCs), one-month post Dose-2 of NTHi-Mcat vaccine ^[1]
End point description: Antibody concentrations as measured by ELISA (Enzyme-linked immunosorbent assay) and expressed as adjusted (ANCOVA model) GMCs in ELISA units per milliliter (EU/mL). Cut-off value for the assay is 153,16,8 and 28 EU/mL for Anti-PD, Anti-PE, Anti-PilA and Anti-UspA2 antibodies respectively. The ANCOVA model includes study group, smoking status (current or former), age category (50-59, 60-69, 70-80 years of age) and center as factors and the antibody concentration before Dose 1 as covariate. Analysis was performed on the per protocol set (PPS) which included all subjects who received full study treatment course to which they were randomized and had post-vaccination immunogenicity data minus subjects with protocol deviations that lead to exclusion. As PPS sample size was not met in Sh_NTHi_Mcat_3 and Sh_NTHi-Mcat_6 groups, those were not part of the analysis and timeframe was adapted. Shingrix-Only Group was not included in this analysis, as subjects didn't receive the NTHi MCAT vaccine.	
End point type	Primary
End point timeframe: At 1 month after dose 2 of NTHi-Mcat vaccine (Day 181, in Sh_NTHi-Mcat_1 group and Day 91 in NTHi-Mcat group)	

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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	NTHi-Mcat Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	118	124		
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PD (N=118;123)	1402.804 (1139.194 to 1727.414)	1489.531 (1203.846 to 1843.014)		
Anti-PE (N=118;124)	6234.827 (5053.049 to 7692.992)	7032.52 (5666.105 to 8728.452)		
Anti-PilA (N=117;124)	1244.373 (963.063 to 1607.854)	1089.799 (840.246 to 1413.47)		
Anti-UspA2 (N=118;124)	1022.961 (894.403 to 1169.998)	941.45 (820.993 to 1079.58)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
To demonstrate the non-inferiority (NI) of the humoral immune response 1 month after Dose 2 of GSK Biologicals' NTHi-Mcat investigational vaccine when administered 1 after Shingrix vaccine versus the humoral immune response 1 month after Dose 2 of GSK Biologicals' NTHi-Mcat investigational vaccine alone.	
Comparison groups	Sh_NTHi-Mcat_1 Group v NTHi-Mcat Group
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	0.942
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.765
upper limit	1.159

Statistical analysis title	Statistical Analysis 2
----------------------------	------------------------

Statistical analysis description:

To demonstrate the non-inferiority (NI) of the humoral immune response 1 month after Dose 2 of GSK Biologicals' NTHi-Mcat investigational vaccine when administered 1 after Shingrix vaccine versus the

humoral immune response 1 month after Dose 2 of GSKBiologicals' NTHi-Mcat investigational vaccine alone.

Comparison groups	Sh_NTHi-Mcat_1 Group v NTHi-Mcat Group
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	0.887
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.719
upper limit	1.093

Statistical analysis title	Statistical Analysis 3
-----------------------------------	------------------------

Statistical analysis description:

To demonstrate the non-inferiority (NI) of the humoral immune response 1 month after Dose 2 of GSK Biologicals' NTHi-Mcat investigational vaccine when administered 1 after Shingrix vaccine versus the humoral immune response 1 month after Dose 2 of GSKBiologicals' NTHi-Mcat investigational vaccine alone.

Comparison groups	Sh_NTHi-Mcat_1 Group v NTHi-Mcat Group
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	1.142
Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.884
upper limit	1.474

Statistical analysis title	Statistical Analysis 4
-----------------------------------	------------------------

Statistical analysis description:

To demonstrate the non-inferiority (NI) of the humoral immune response 1 month after Dose 2 of GSK Biologicals' NTHi-Mcat investigational vaccine when administered 1 after Shingrix vaccine versus the humoral immune response 1 month after Dose 2 of GSKBiologicals' NTHi-Mcat investigational vaccine alone.

Comparison groups	Sh_NTHi-Mcat_1 Group v NTHi-Mcat Group
Number of subjects included in analysis	242
Analysis specification	Pre-specified
Analysis type	
Method	ANCOVA
Parameter estimate	GMC ratio
Point estimate	1.087

Confidence interval	
level	Other: 0.95 %
sides	2-sided
lower limit	0.948
upper limit	1.245

Secondary: Anti-PD, Anti-PE, Anti-PiIA, Anti-UspA2 antibody concentrations in terms of GMCs, before first NTHi-Mcat vaccine

End point title	Anti-PD, Anti-PE, Anti-PiIA, Anti-UspA2 antibody concentrations in terms of GMCs, before first NTHi-Mcat vaccine ^[2]
-----------------	---

End point description:

GMCs and their 95% CI for each of the antibodies, as measured by ELISA, were calculated (the GMCs were computed by taking the Anti-log of the mean of the log concentration transformations). Analysis was performed on the PPS which included all subjects who received full study treatment course to which they were randomized and had post-vaccination immunogenicity data minus subjects with protocol deviations that lead to exclusion. Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

Before the first dose of NTHi-Mcat vaccine (Day 91, Day 151 and Day 241 for Sh_NTHi-Mcat_1, Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6 group, respectively, and Day 1 for NTHi-Mcat group)

Notes:

[2] - 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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	96	73	124
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PD (N=118;95;73;124)	94.7 (86.2 to 104.1)	105.1 (89.8 to 123)	95.6 (84.5 to 108.3)	105.3 (93.4 to 118.6)
Anti-PE (N=118;96;73;123)	22 (18 to 26.9)	21.2 (17.6 to 25.4)	18.6 (14.3 to 24.2)	23.9 (19.8 to 28.9)
Anti-PiIA (N=118;96;73;124)	7.8 (6.6 to 9.3)	10.5 (8.2 to 13.5)	9.7 (7.5 to 12.6)	9.1 (7.5 to 11)
Anti-UspA2 (N=118;96;73;124)	352.4 (292.5 to 424.7)	343 (286.3 to 411)	440.3 (343.5 to 564.5)	521.4 (441 to 616.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PD, Anti-PE, Anti-PiIA, Anti-UspA2 antibody concentrations in terms of GMCs, one-month post Dose-2 of NTHi-Mcat vaccine

End point title	Anti-PD, Anti-PE, Anti-PiIA, Anti-UspA2 antibody concentrations in terms of GMCs, one-month post Dose-2 of NTHi-Mcat vaccine ^[3]
-----------------	---

End point description:

GMCs and their 95% CI for each of the antibodies, as measured by ELISA, were calculated (the GMCs were computed by taking the Anti-log of the mean of the log concentration transformations) before the first dose of NTHi-Mcat vaccine. Analysis was performed on the PPS which included all subjects who received full study treatment course to which they were randomized and had post-vaccination immunogenicity data minus subjects with protocol deviations that lead to exclusion. Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

At one month after the second dose of NTHi-Mcat vaccine (Day 181, 241, 331 in the Sh_NTHi-Mcat_1, Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6 group, respectively, and Day 91 in the NTHi-Mcat group)

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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	96	73	124
Units: EU/mL				
geometric mean (confidence interval 95%)				
Anti-PD (N=118;96;73;123)	1496.7 (1272.7 to 1760.1)	1504 (1209.9 to 1869.6)	1539 (1277.3 to 1854.2)	1683.5 (1434.5 to 1975.5)
Anti-PE (N=118;96;73;124)	5911.8 (5121.3 to 6824.3)	5920.8 (4868.4 to 7200.8)	6048.5 (4943.3 to 7400.8)	6562.4 (5660.9 to 7607.5)
Anti-PilA (N=117;96;73;124)	1089.3 (910.3 to 1303.4)	1030.6 (839.4 to 1265.3)	1114.7 (864.9 to 1436.6)	999.3 (830.3 to 1202.7)
Anti-UspA2 (N=118;96;73;124)	926.8 (796.6 to 1078.4)	942.2 (819.6 to 1083.2)	1289.2 (1062.5 to 1564.5)	1066.4 (946.6 to 1201.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of seropositive subjects for Anti-PD, Anti-PE, Anti-PilA, Anti-UspA2 antibodies before first NTHi-Mcat vaccine

End point title	Percentage of seropositive subjects for Anti-PD, Anti-PE, Anti-PilA, Anti-UspA2 antibodies before first NTHi-Mcat vaccine ^[4]
-----------------	--

End point description:

A seropositive subject is defined as a subject whose Anti-PD, Anti-PE, Anti-PilA and Anti-UspA2 antibody concentrations are greater than or equal to the assay cut-off value. Seropositivity rates with 95% CI is defined using the assay lower limit of quantification (LLOQ). Cut-off value for the assay is 153, 16, 8 and 28 EU/mL for Anti-PD, Anti-PE, Anti-PilA and Anti-UspA2 antibodies respectively. Analysis was performed on the PPS which included all subjects who received full study treatment course to which they were randomized and had post-vaccination immunogenicity data minus subjects with protocol deviations that lead to exclusion. Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

Before the first dose of NTHi-Mcat vaccine (Day 91, Day 151 and Day 241 in the Sh_NTHi-Mcat_1,

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	96	73	124
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-PD (N=118;95;73;124)	16.9 (10.7 to 25)	20 (12.5 to 29.5)	19.2 (10.9 to 30.1)	21.8 (14.9 to 30.1)
Anti-PE (N=118;96;73;123)	57.6 (48.2 to 66.7)	63.5 (53.1 to 73.1)	50.7 (38.7 to 62.6)	61.8 (52.6 to 70.4)
Anti-PilA (N=118;96;73;124)	38.1 (29.4 to 47.5)	49 (38.6 to 59.4)	47.9 (36.1 to 60)	43.5 (34.7 to 52.7)
Anti-UspA2 (N=118;96;73;124)	100 (96.9 to 100)	100 (96.2 to 100)	100 (95.1 to 100)	100 (97.1 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects seropositive for Anti-PD, Anti-PE, Anti-PilA, Anti-UspA2 antibodies, one-month post Dose-2 of NTHi-Mcat vaccine

End point title	Percentage of subjects seropositive for Anti-PD, Anti-PE, Anti-PilA, Anti-UspA2 antibodies, one-month post Dose-2 of NTHi-Mcat vaccine ^[5]
-----------------	---

End point description:

A seropositive subject is defined as a subject whose Anti-PD, Anti-PE, Anti-PilA and Anti-UspA2 antibody concentrations are greater than or equal to the assay cut-off value. Seropositivity rates with 95% CI are defined using the assay (LLOQ). Cut-off value for the assay is 153, 16, 8 and 28 EU/mL for Anti-PD, Anti-PE, Anti-PilA and Anti-UspA2 antibodies respectively. Analysis was performed on the PPS which included all subjects who received full study treatment course to which they were randomized and had post-vaccination immunogenicity data minus subjects with protocol deviations that lead to exclusion. Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

At one month after the second dose of NTHi-Mcat vaccine (Day 181, 241, 331 in the Sh_NTHi-Mcat_1, Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6 group, respectively, and Day 91 in the NTHi-Mcat group)

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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	118	96	73	124
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-PD (N=118;96;73;123)	99.2 (95.4 to 100)	97.9 (92.7 to 99.7)	100 (95.1 to 100)	100 (97 to 100)
Anti-PE (N=118;96;73;124)	100 (96.9 to 100)	100 (96.2 to 100)	100 (95.1 to 100)	100 (97.1 to 100)
Anti-PilA (N=117;96;73;124)	100 (96.9 to 100)	100 (96.2 to 100)	100 (95.1 to 100)	100 (97.1 to 100)
Anti-UspA2 (N=118;96;73;124)	100 (96.9 to 100)	100 (96.2 to 100)	100 (95.1 to 100)	100 (97.1 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of specific Cluster of Differentiation 4 (CD4+) T-cells against NTHi and Mcat antigens for evaluation of cell-mediated immune (CMI) response, before first dose of NTHi-Mcat vaccine

End point title	Frequency of specific Cluster of Differentiation 4 (CD4+) T-cells against NTHi and Mcat antigens for evaluation of cell-mediated immune (CMI) response, before first dose of NTHi-Mcat vaccine ^[6]
-----------------	---

End point description:

Frequency of specific CD4+ T-cells was measured by flow cytometry intracellular cytokine staining (ICS) expressing at least 2 different markers among CD40 Ligand (CD40L), interleukin (IL)-2, IL-13, IL-17, tumour necrosis factor alpha (TNF-α) and interferon gamma (IFN-γ), upon in vitro stimulation. Analysis was performed on Cell-Mediated immune (CMI) sub-cohort, which included approximately 60 subjects (15/each group), for which an additional blood sample was taken at each pre-defined timepoint (sub-cohort selected from sites able to process the blood samples according to GSK procedures for peripheral blood mononuclear cell preparation). Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

Before the first dose of NTHi-Mcat vaccine (Day 91, Day 151 and Day 241 in the Sh_NTHi-Mcat_1, Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6 group, respectively, and Day 1 in the NTHi-Mcat group)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	12	3	13
Units: CD4+ T cells/million cells				
arithmetic mean (standard deviation)				
M catarrhalis.UspA2 - CD4+ T-cells (N=10;12;3;13)	112.945 (± 153.903)	101.739 (± 94.932)	81.578 (± 90.919)	92.685 (± 99.661)
NTHi.PD - CD4+ T-cells (N=10;12;3;13)	89.456 (± 68.929)	59.522 (± 82.06)	36.439 (± 57.347)	96.893 (± 74.87)

NTHi.PE - CD4+ T-cells (N=10;12;3;13)	79.838 (± 58.999)	46.112 (± 63.007)	69.546 (± 97.09)	80.717 (± 119.316)
NTHi.PiIA - CD4+ T-cells (N=10;12;3;13)	61.627 (± 53.613)	42.438 (± 55.575)	60.139 (± 51.37)	105.558 (± 97.618)

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of CD4+ T-cells against NTHi and Mcat antigens for evaluation of CMI response, at one-month post dose 2 of NTHi-Mcat vaccine

End point title	Frequency of CD4+ T-cells against NTHi and Mcat antigens for evaluation of CMI response, at one-month post dose 2 of NTHi-Mcat vaccine ^[7]
-----------------	---

End point description:

Frequency of specific CD4+ T-cells was measured by flow cytometry ICS expressing at least 2 different markers among CD40L, IL-2, IL-13, IL-17, TNF-α and IFN-γ, upon in vitro stimulation. Analysis was performed on CMI sub-cohort, which included approximately 60 subjects (15/each group), for which an additional blood sample was taken at each pre-defined time point (sub-cohort selected from sites able to process the blood samples according to GSK procedures for peripheral blood mononuclear cell preparation). Subjects from the Shingrix-Only Group were not included in this analysis, as they didn't receive the NTHi MCAT vaccine.

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

End point timeframe:

At one month after second dose of NTHi-Mcat vaccine (Day 181, Day 241 and Day 331 in the Sh_NTHi-Mcat_1, Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6 group, respectively, and Day 91 in the NTHi-Mcat group)

Notes:

[7] - 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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	11	3	13
Units: CD4+ T cells/million cells				
arithmetic mean (standard deviation)				
M catarrhalis.UspA2 - CD4+ T-cells (N=10;11;3;13)	721.851 (± 457.94)	619.68 (± 392.133)	1001.839 (± 144.057)	735.177 (± 471.515)
NTHi.PD - CD4+ T-cells (N=10;11;3;13)	632.849 (± 323.731)	527.26 (± 281.827)	1570.631 (± 1064.327)	742.666 (± 527.567)
NTHi.PE - CD4+ T-cells (N=10;11;3;13)	565.964 (± 411.715)	581.338 (± 520.594)	888.057 (± 154.524)	1155.341 (± 699.841)
NTHi.PiIA - CD4+ T-cells (N=10;11;3;13)	332.43 (± 273.215)	318.46 (± 195.527)	333.501 (± 121.712)	388.282 (± 207.434)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with reported solicited local adverse event (AE)

End point title	Percentage of subjects with reported solicited local adverse event (AE) ^[8]
End point description: The percentage of subjects with at least one local solicited AE, regardless of intensity, during the 7-day follow-up period after each NTHi-Mcat vaccine dose, are reported by study group. Assessed local symptoms were pain, redness and swelling. Any local injection site redness/swelling is scored as follows: diameter >=20 milli-meters. Analysis was performed on the Solicited safety set (SSS) which included all subjects who received at least 1 dose of the study treatment and who have solicited safety data.	
End point type	Secondary
End point timeframe: During the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after Dose 1 and after Dose 2 of NTHi-Mcat vaccine	

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	133	118	135
Units: Percentage of subjects				
number (confidence interval 95%)				
Erythema (mm), Dose 1 (N=134;133;118;135)	6 (2.6 to 11.4)	15 (9.4 to 22.3)	11 (6 to 18.1)	12.6 (7.5 to 19.4)
Erythema (mm), Dose 2 (N=133;131;117;127)	12.8 (7.6 to 19.7)	13.7 (8.4 to 20.8)	17.9 (11.5 to 26.1)	11.8 (6.8 to 18.7)
Pain, Dose 1 (N=134;133;118;135)	59.7 (50.9 to 68.1)	69.2 (60.6 to 76.9)	61 (51.6 to 69.9)	63.7 (55 to 71.8)
Pain, Dose 2 (N=133;131;117;127)	69.9 (61.4 to 77.6)	76.3 (68.1 to 83.3)	72.6 (63.6 to 80.5)	75.6 (67.2 to 82.8)
Swelling (mm), Dose 1 (N=134;133;118;135)	3.7 (1.2 to 8.5)	10.5 (5.9 to 17)	5.9 (2.4 to 11.8)	5.2 (2.1 to 10.4)
Swelling (mm), Dose 2 (N=133;131;117;127)	7.5 (3.7 to 13.4)	8.4 (4.3 to 14.5)	6.8 (3 to 13)	7.9 (3.8 to 14)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with reported solicited general AE

End point title	Percentage of subjects with reported solicited general AE ^[9]
End point description: The percentage of subjects with at least one general solicited AE, regardless of intensity, during the 7-day follow-up period after each NTHi-Mcat vaccine dose, are reported by study group. Assessed solicited general symptoms were Fatigue, Gastrointestinal symptoms (nausea, vomiting, diarrhoea and/or abdominal pain), Headache, Myalgia, Chills and Fever (oral cavity or axillary route - temperature equal or higher than [\geq] 37.5 degrees Celsius [$^{\circ}\text{C}$]). Analysis was performed on the SSS which included all subjects who received at least 1 dose of the study treatment and who have solicited safety data.	
End point type	Secondary
End point timeframe: During the 7-day follow-up period (i.e. day of vaccination and 6 subsequent days) after Dose 1 and after Dose 2 of NTHi-Mcat vaccine	

Notes:

[9] - 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: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	133	118	135
Units: Percentage of subjects				
number (confidence interval 95%)				
Chills, Dose 1 (N=134;133;118;35)	11.9 (7 to 18.7)	12 (7 to 18.8)	16.9 (10.7 to 25)	7.4 (3.6 to 13.2)
Chills, Dose 2 (N=133;131;117;127)	25.6 (18.4 to 33.8)	26 (18.7 to 34.3)	22.2 (15.1 to 30.8)	16.5 (10.5 to 24.2)
Fatigue, Dose 1 (N=134;133;118;135)	26.1 (18.9 to 34.4)	38.3 (30.1 to 47.2)	39 (30.1 to 48.4)	34.1 (26.1 to 42.7)
Fatigue, Dose 2 (N=133;131;117;127)	39.1 (30.8 to 47.9)	48.1 (39.3 to 57)	43.6 (34.4 to 53.1)	37.8 (29.3 to 46.8)
Fever (C), Dose 1 (N=134;133;118;135)	1.5 (0.2 to 5.3)	1.5 (0.2 to 5.3)	2.5 (0.5 to 7.3)	3 (0.8 to 7.4)
Fever (C), Dose 2 (N=133;131;117;127)	11.3 (6.5 to 17.9)	8.4 (4.3 to 14.5)	8.5 (4.2 to 15.2)	8.7 (4.4 to 15)
Gastrointest. symptoms, Dose 1 (N=134;133;118;135)	13.4 (8.2 to 20.4)	13.5 (8.2 to 20.5)	16.1 (10 to 24)	13.3 (8.1 to 20.3)
Gastrointest. symptoms, Dose 2 (N=133;131;117;127)	15.8 (10 to 23.1)	15.3 (9.6 to 22.6)	12.8 (7.4 to 20.3)	9.4 (5 to 15.9)
Headache, Dose 1 (N=134;133;118;135)	20.9 (14.4 to 28.8)	26.3 (19.1 to 34.7)	22.9 (15.7 to 31.5)	18.5 (12.4 to 26.1)
Headache, Dose 2 (N=133;131;117;127)	32.3 (24.5 to 41)	38.2 (29.8 to 47.1)	23.9 (16.5 to 32.7)	22 (15.2 to 30.3)
Myalgia, Dose 1 (N=134;133;118;135)	20.1 (13.7 to 27.9)	23.3 (16.4 to 31.4)	25.4 (17.9 to 34.3)	27.4 (20.1 to 35.7)
Myalgia, Dose 2 (N=133;131;117;127)	33.1 (25.2 to 41.8)	37.4 (29.1 to 46.3)	36.8 (28 to 46.2)	37.8 (29.3 to 46.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with any unsolicited AE

End point title	Percentage of subjects with any unsolicited AE ^[10]
End point description:	
An unsolicited adverse event is an adverse event that was not solicited using a Subject Diary and that was spontaneously communicated by a subject who has signed the informed consent. The percentage of subjects with at least one unsolicited AE, regardless of intensity or relationship to vaccination, during the 30-day follow-up period after any NTHi-Mcat vaccine dose are reported for each group. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms is reported as an unsolicited adverse event. Analysis was performed on the Unsolicited safety set which included all subjects who receive at least 1 dose of the study treatment and who have unsolicited safety data.	
End point type	Secondary
End point timeframe:	
During the 30-day follow-up period (i.e. day of vaccination and 29 subsequent days) after Dose 1 and after Dose 2 of NTHi-Mcat vaccine	

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Scope of this endpoint analysis was descriptive. Therefore, no statistical analyses apply for this endpoint.

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	134	122	135
Units: Percentage of subjects				
number (confidence interval 95%)				
Dose 1 (N=134;134;122;135)	13.4 (8.2 to 20.4)	14.9 (9.4 to 22.1)	11.5 (6.4 to 18.5)	18.5 (12.4 to 26.1)
Dose 2 (N=133;131;118;129)	15 (9.4 to 22.3)	15.3 (9.6 to 22.6)	8.5 (4.1 to 15)	10.9 (6.1 to 17.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with any serious adverse event (SAE) during Epoch 001

End point title	Percentage of subjects with any serious adverse event (SAE) during Epoch 001
-----------------	--

End point description:

The percentage of subjects with at least one SAE, regardless of intensity or relationship to vaccination, from Day 1 up to and including Day 331, were reported for each group. An SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject or was a congenital anomaly/birth defect in the offspring of a study subject. AE(s) considered as SAE(s) also include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, as per the medical or scientific judgement of the physician. Analysis was performed on the Exposed Set (ES) which included all subjects who received at least 1 dose of the study treatment.

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

End point timeframe:

From Day 1 up to and including Day 331 (Epoch 001)

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	134	122	135
Units: Percentage of subjects				
number (confidence interval 95%)	4.5 (1.7 to 9.5)	3.7 (1.2 to 8.5)	2.5 (0.5 to 7)	1.5 (0.2 to 5.2)

End point values	Shingrix-Only			
------------------	---------------	--	--	--

	Group			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percentage of subjects				
number (confidence interval 95%)	6.3 (0.2 to 30.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with any Potential Immune-mediated diseases (pIMD's) during Epoch 001

End point title	Percentage of subjects with any Potential Immune-mediated diseases (pIMD's) during Epoch 001
-----------------	--

End point description:

pIMD's are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. Analysis was performed on the ES which included all subjects who received at least 1 dose of the study treatment.

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

End point timeframe:

From Day 1 up to and including Day 331 (Epoch 001)

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	134	134	122	135
Units: Percentage of subjects				
number (confidence interval 95%)	0 (0 to 2.7)	1.5 (0.2 to 5.3)	0.8 (0 to 4.5)	0 (0 to 2.7)

End point values	Shingrix-Only Group			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: Percentage of subjects				
number (confidence interval 95%)	12.5 (1.6 to 38.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with any SAE during Epoch 002

End point title	Percentage of subjects with any SAE during Epoch 002
End point description:	
The percentage of subjects with at least one SAE, regardless of intensity or relationship to vaccination, from Day 331 up to and including Day 661, are reported for each group. An SAE is defined as any untoward medical occurrence that resulted in death, was life-threatening, requires hospitalization or prolongation of hospitalization, resulted in disability/incapacity in a subject or was a congenital anomaly/birth defect in the offspring of a study subject. AE(s) considered as SAE(s) also include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, as per the medical or scientific judgement of the physician. Epoch 2 data analysis is not achieved at the time of the posting. Results will be added when available.	
End point type	Secondary
End point timeframe:	
From Day 331 up to and including Day 661 (Epoch 002)	

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[11]	0 ^[12]	0 ^[13]	0 ^[14]
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[11] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[12] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[13] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[14] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

End point values	Shingrix-Only Group			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[15]			
Units: Percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[15] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with any pIMD's during Epoch 002

End point title	Percentage of subjects with any pIMD's during Epoch 002
End point description:	
pIMD's are a subset of AEs that include autoimmune diseases and other inflammatory and/or neurologic disorders of interest which may or may not have an autoimmune aetiology. Epoch 2 data analysis is not achieved at the time of the posting. Results will be added when available.	
End point type	Secondary
End point timeframe:	
From Day 331 up to and including Day 661 (Epoch 002)	

End point values	Sh_NTHi-Mcat_1 Group	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_6 Group	NTHi-Mcat Group
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0 ^[16]	0 ^[17]	0 ^[18]	0 ^[19]
Units: Percentage of subjects				
number (confidence interval 95%)	(to)	(to)	(to)	(to)

Notes:

[16] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[17] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[18] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

[19] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

End point values	Shingrix-Only Group			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[20]			
Units: Percentage of subjects				
number (confidence interval 95%)	(to)			

Notes:

[20] - Epoch 2 data analysis is not achieved at the time of posting. Results will be added when available.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited adverse events were collected during the 7-day follow-up period and unsolicited adverse events during the 30-day follow-up period. Serious adverse events were collected from Day 1 up to Day 331.

Adverse event reporting additional description:

Other Adverse events were not collected for Shingrix-Only Group.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	23.1
--------------------	------

Reporting groups

Reporting group title	Sh_NTHi-Mcat_3 Group
-----------------------	----------------------

Reporting group description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 3-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 151 and Day 211.

Reporting group title	Sh_NTHi-Mcat_1 Group
-----------------------	----------------------

Reporting group description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, and following a 1-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 91, and Day 151.

Reporting group title	NTHi-Mcat Group
-----------------------	-----------------

Reporting group description:

Subjects enrolled in this group received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart, at Day 1 and Day 61.

Reporting group title	Shingrix-Only Group
-----------------------	---------------------

Reporting group description:

Subjects enrolled in this group received at least 1, maximum 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61, but didn't receive any dose of NTHi-Mcat investigational vaccine.

Reporting group title	Sh_NTHi-Mcat_6 Group
-----------------------	----------------------

Reporting group description:

Subjects enrolled in this group received 2 doses of GSK Biologicals' Shingrix vaccine at Day 1 and Day 61 and, following a 6-month gap, subjects received 2 doses of GSK Biological's NTHi-Mcat investigational vaccine 2 months apart at Day 241 and Day 301.

Serious adverse events	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_1 Group	NTHi-Mcat Group
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 134 (3.73%)	6 / 134 (4.48%)	2 / 135 (1.48%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			

subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (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 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (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
Lung neoplasm malignant			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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
Lymphoma			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (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
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (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
Peripheral artery restenosis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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

Atrial fibrillation			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (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			
Ruptured cerebral aneurysm			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (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
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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
COVID-19			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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
Tuberculosis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (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	Shingrix-Only Group	Sh_NTHi-Mcat_6 Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	3 / 122 (2.46%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 16 (6.25%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoma			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery restenosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ruptured cerebral aneurysm			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin necrosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			

subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Sh_NTHi-Mcat_3 Group	Sh_NTHi-Mcat_1 Group	NTHi-Mcat Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 134 (93.28%)	118 / 134 (88.06%)	125 / 135 (92.59%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Dental implantation			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Chest discomfort			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	2	0
Chest pain			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	41 / 134 (30.60%)	40 / 134 (29.85%)	26 / 135 (19.26%)
occurrences (all)	50	50	31
Discomfort			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	78 / 134 (58.21%)	63 / 134 (47.01%)	65 / 135 (48.15%)
occurrences (all)	114	88	95
Feeling hot			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Hangover			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	27 / 134 (20.15%)	21 / 134 (15.67%)	24 / 135 (17.78%)
occurrences (all)	38	25	32
Injection site movement impairment			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Injection site pain			
subjects affected / exposed	112 / 134 (83.58%)	105 / 134 (78.36%)	112 / 135 (82.96%)
occurrences (all)	192	173	182
Injection site pruritus			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Injection site swelling			

subjects affected / exposed occurrences (all)	19 / 134 (14.18%) 25	12 / 134 (8.96%) 15	15 / 135 (11.11%) 17
Malaise subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Pyrexia subjects affected / exposed occurrences (all)	12 / 134 (8.96%) 13	16 / 134 (11.94%) 17	14 / 135 (10.37%) 15
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Respiratory, thoracic and mediastinal disorders Asthmatic crisis subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Catarrh subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	1 / 134 (0.75%) 1	1 / 135 (0.74%) 1
Cough subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	3 / 134 (2.24%) 3	2 / 135 (1.48%) 2
Dysphonia subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	1 / 134 (0.75%) 1	0 / 135 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Nasal congestion subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Productive cough subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	2 / 134 (1.49%) 2	0 / 135 (0.00%) 0
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	1 / 134 (0.75%) 1	1 / 135 (0.74%) 1
Investigations Weight increased subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Injury, poisoning and procedural complications Arthropod bite subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Fall subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Head injury subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	1 / 135 (0.74%) 1
Joint dislocation subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Ligament rupture subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Lower limb fracture			

subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Muscle rupture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Thermal burn			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Tibia fracture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	66 / 134 (49.25%)	56 / 134 (41.79%)	42 / 135 (31.11%)
occurrences (all)	92	78	56
Somnolence			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	0	1	2
Ear pruritus			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Chalazion			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Eyelid ptosis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Swelling of eyelid			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	1 / 135 (0.74%)
occurrences (all)	0	1	1
Constipation			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	2	1	0
Dyspepsia			

subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	3	0	0
Gastrointestinal disorder			
subjects affected / exposed	32 / 134 (23.88%)	34 / 134 (25.37%)	26 / 135 (19.26%)
occurrences (all)	38	39	30
Nausea			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Tooth disorder			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	0	0	2

Psoriasis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	1	0	1
Urticaria			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 134 (2.24%)	2 / 134 (1.49%)	1 / 135 (0.74%)
occurrences (all)	3	2	1
Arthritis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	3 / 135 (2.22%)
occurrences (all)	1	1	3
Intervertebral disc disorder			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Muscle contracture			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	64 / 134 (47.76%)	48 / 134 (35.82%)	67 / 135 (49.63%)
occurrences (all)	80	73	87
Neck pain			

subjects affected / exposed	3 / 134 (2.24%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	4	0	0
Osteoarthritis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Infections and infestations			
Bacterial vaginosis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	1 / 134 (0.75%)	3 / 134 (2.24%)	0 / 135 (0.00%)
occurrences (all)	1	3	0
Cystitis			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	0	0	0
Dengue fever			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Genital herpes			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	1	1	0

Nasopharyngitis			
subjects affected / exposed	3 / 134 (2.24%)	3 / 134 (2.24%)	0 / 135 (0.00%)
occurrences (all)	3	3	0
Oral herpes			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	1
Otitis media			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Pulpitis dental			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	3 / 135 (2.22%)
occurrences (all)	1	1	3
Schistosomiasis cutaneous			
subjects affected / exposed	0 / 134 (0.00%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	2 / 135 (1.48%)
occurrences (all)	1	0	2
Tooth abscess			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	1 / 135 (0.74%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 134 (0.75%)	0 / 134 (0.00%)	0 / 135 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 134 (0.75%)	1 / 134 (0.75%)	0 / 135 (0.00%)
occurrences (all)	1	1	0
Viral infection			
subjects affected / exposed	0 / 134 (0.00%)	0 / 134 (0.00%)	3 / 135 (2.22%)
occurrences (all)	0	0	3

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 134 (0.75%) 1	0 / 134 (0.00%) 0	0 / 135 (0.00%) 0
Metabolism and nutrition disorders Metabolic syndrome subjects affected / exposed occurrences (all)	0 / 134 (0.00%) 0	1 / 134 (0.75%) 1	0 / 135 (0.00%) 0

Non-serious adverse events	Shingrix-Only Group	Sh_NTHi-Mcat_6 Group	
Total subjects affected by non-serious adverse events subjects affected / exposed	0 / 16 (0.00%)	107 / 122 (87.70%)	
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Surgical and medical procedures Dental implantation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Chest discomfort subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Chest pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 122 (1.64%) 2	
Chills subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	40 / 122 (32.79%) 47	
Discomfort subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Fatigue			

subjects affected / exposed	0 / 16 (0.00%)	68 / 122 (55.74%)	
occurrences (all)	0	99	
Feeling hot			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Hangover			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Injection site erythema			
subjects affected / exposed	0 / 16 (0.00%)	28 / 122 (22.95%)	
occurrences (all)	0	34	
Injection site movement impairment			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	0 / 16 (0.00%)	98 / 122 (80.33%)	
occurrences (all)	0	157	
Injection site pruritus			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Injection site swelling			
subjects affected / exposed	0 / 16 (0.00%)	13 / 122 (10.66%)	
occurrences (all)	0	15	
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 16 (0.00%)	13 / 122 (10.66%)	
occurrences (all)	0	13	
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	

Respiratory, thoracic and mediastinal disorders			
Asthmatic crisis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Catarrh			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Cough			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Dyspnoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Epistaxis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Rhinitis allergic			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Investigations			

Weight increased subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Injury, poisoning and procedural complications			
Arthropod bite subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Fall subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Head injury subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Joint dislocation subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Ligament rupture subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Ligament sprain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Lower limb fracture subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Muscle rupture subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Procedural pain subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Thermal burn subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Tibia fracture			

subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Cardiac disorders Extrasystoles subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Nervous system disorders Balance disorder subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Somnolence subjects affected / exposed occurrences (all) Syncope subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	0 / 122 (0.00%) 0 0 / 122 (0.00%) 0 44 / 122 (36.07%) 59 0 / 122 (0.00%) 0 0 / 122 (0.00%) 0	
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) Ear pruritus subjects affected / exposed occurrences (all) Vertigo subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0 0 / 16 (0.00%) 0	0 / 122 (0.00%) 0 0 / 122 (0.00%) 0 0 / 122 (0.00%) 0	
Eye disorders Blepharospasm subjects affected / exposed occurrences (all) Chalazion	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	

subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Eye pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Eyelid ptosis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Swelling of eyelid			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Gastritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorder			
subjects affected / exposed	0 / 16 (0.00%)	26 / 122 (21.31%)	
occurrences (all)	0	34	
Nausea			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Tooth disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	

Toothache subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	2 / 122 (1.64%) 2	
Skin and subcutaneous tissue disorders Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Eczema subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Erythema subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Pain of skin subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Pruritus subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Psoriasis subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Rash subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	1 / 122 (0.82%) 1	
Urticaria subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Endocrine disorders Basedow's disease subjects affected / exposed occurrences (all)	0 / 16 (0.00%) 0	0 / 122 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Arthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Intervertebral disc disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Muscle contracture			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Myalgia			
subjects affected / exposed	0 / 16 (0.00%)	56 / 122 (45.90%)	
occurrences (all)	0	76	
Neck pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Osteoarthritis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Tendonitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Bacterial vaginosis			

subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Bronchitis		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Cystitis		
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)
occurrences (all)	0	1
Dengue fever		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Gastroenteritis		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Genital herpes		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Herpes simplex		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Influenza		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Nasopharyngitis		
subjects affected / exposed	0 / 16 (0.00%)	2 / 122 (1.64%)
occurrences (all)	0	2
Oral herpes		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Otitis media		
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)
occurrences (all)	0	0
Pulpitis dental		
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)
occurrences (all)	0	1
Respiratory tract infection		

subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Schistosomiasis cutaneous			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	1 / 122 (0.82%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Viral infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Metabolic syndrome			
subjects affected / exposed	0 / 16 (0.00%)	0 / 122 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 May 2020	<ul style="list-style-type: none">•The current analysis of the primary objective is planned on the per protocol population. The use of the per protocol defined windows for vaccination and blood draws minimizes potential variability within the data for statistical comparisons. To control the type I error below 2.5% (one-sided), a sequential procedure is planned in the protocol. Starting from the 6-months lag, the 3-months NI will be tested only if the 6-months NI will be demonstrated, while the 1-month NI will be tested only if the 6-months and 3-months NI will be both demonstrated.•The study started on 23 Apr 2019. At the time of writing, group Sh_NTHi-Mcat_1 and control group NTHi-Mcat have completed the vaccination schedule and the blood draw as dictated by the study protocol, whereas the less advanced groups (Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6) are either due to receive the study vaccine or to undergo a blood draw. In accordance with the safety measures applied for COVID-19 containment in the countries where the study is conducted, a number of study visits are unlikely to occur as planned. This is expected to impact 2 of the study groups (Sh_NTHi-Mcat_3 and Sh_NTHi-Mcat_6).•The amendment includes a modified primary objective, should the Sh-NTHi-Mcat_6 or the Sh-NTHi-Mcat_3 and Sh_NTHi-Mcat_3 groups not meet the per-protocol defined sample size.•This amendment also outlines measures (e.g. for safety monitoring) that may be applicable during special circumstances, like COVID-19 pandemic.•Provisions relating to specific reporting of serious adverse events and serious adverse reactions, in accordance with Article R1123-54 and Article R1123-46 of the French Public Health Code, are incorporated into the "Requirements for France" Section of this Protocol Amendment.•Other minor changes have been made to correct typos and improve clarity and alignment within the document.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported