Clinical trial results:
A Phase 1b/2 Randomised, Placebo-controlled, Dose-ranging Study to Evaluate Safety, Tolerability and Immunogenicity of a Chimpanzee Adenovirus (ChAdOx1)-vectored Multigenotype High Risk Human Papillomavirus (hrHPV) Vaccine and Modified Vaccinia Ankara (MVA)-vectored Multigenotype hrHPV Vaccine in Women with Low-grade HPV-related Cervical Lesions

Summary

EudraCT number	2019-001890-98
Trial protocol	GB BE
Global end of trial date	15 February 2024

Results information

Result version number	v1 (current)
This version publication date	22 March 2025
First version publication date	22 March 2025

Trial information

Trial identification

Sponsor protocol code	HPV001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04607850
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Barinthus Biotherapeutics UK Ltd
Sponsor organisation address	Units 6 to 10, Oxford, United Kingdom, OX11 0DF
Public contact	Chief Medical Officer, Leon Hooftman, Barinthus Biotherapeutics UK Ltd, +44 1865818808, clinicaltrials@barinthusbio.com
Scientific contact	Chief Medical Officer, Leon Hooftman, Barinthus Biotherapeutics UK Ltd, +44 1865818808, clinicaltrials@barinthusbio.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	23 October 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2024
Global end of trial reached?	Yes
Global end of trial date	15 February 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety and tolerability of ChAdOx1-HPV plus MVA-HPV vaccines when administered in a prime boost regimen.

Protection of trial subjects:

The trial focused on hrHPV-positive participants with low-grade cervical lesions, reflecting the standard care of monitoring rather than immediate intervention. A lead-in phase with a dose-escalation design in a small participant group minimized exposure to poorly tolerated doses. Safety and tolerability data were reviewed at each dose adjustment, with an additional review before transitioning to the main phase.

The main phase used a parallel-group, randomised, placebo-controlled design to assess dose-dependent safety, efficacy, and immunogenicity, with treatments administered in a blinded fashion to minimize bias. Standard safety assessments included monitoring adverse events, lab tests, vital signs, and physical exams. Participants reported foreseeable adverse events via an eDiary for 3 days post-dose, supplemented by in-clinic assessments.

Defined grading scales assessed symptom severity and lab abnormalities, with pre-established trial stopping/holding criteria triggering Data Monitoring Committee (DMC) reviews. Individual stopping criteria allowed for participant withdrawal if needed. Diagnostic procedures, including colposcopy with biopsy, HPV swabbing, and cervical cytobrush sampling, followed established clinical standards to ensure participant safety and accurate monitoring throughout the trial.

Background therapy:

N/A

Evidence for comparator:

The placebo was 0.9% normal saline. The parallel-group, randomised, placebo-controlled design used in the main phase was used to allow for an examination of any dose-dependent effects on safety, efficacy and
immunogenicity and compared to placebo. This design made it possible to obtain unbiased inferences about differences between treatments. Treatments were administered in a blinded fashion with the Sponsor, CRO, Investigator, trial team members performing safety assessments beyond randomisation and participant unaware of the treatment identity to further minimise any potential bias in the overall assessment.

Actual start date of recruitment	16 March 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason, Regulatory reason, Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 49
Country: Number of subjects enrolled	Belgium: 39
Country: Number of subjects enrolled	Estonia: 20
Worldwide total number of subjects	108
EEA total number of subjects	59

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)	108
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This multicentre trial of VTP-200 had 3 phases across 16 European sites. The lead-in phase (9 participants) tested dose escalation. The main phase (99 participants) compared different doses of ChAdOx1-HPV and MVA-HPV to placebo. The expansion phase was planned but cancelled after Month 12 data analysis showed no clear efficacy signal.

Pre-assignment

Screening details:

Participants were screened between Day -42 and Day -1, with consent obtained before procedures. They received either ChAdOx1-HPV on Day 0 and MVA-HPV on Day 28 or placebo on both days, depending on their phase and group allocation.

Period 1

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

Blinding implementation details:

In the main phase, participants, safety assessors, and most trial team members were blinded to treatment. Staff preparing and administering the drug, an unblinded CRO pharmacy monitor, and the statistician handling randomisation and interim analyses were not blinded. Blinding was preserved through strict procedures in the Site Blinding Plan and Pharmacy Manual, with separate filing systems preventing access to treatment allocations by blinded staff.

Arms

Are arms mutually exclusive?	Yes
Arm title	Main Phase Group 1

Arm description:

Main Phase Group 1, ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV 2 x 10^9 vp and MVA-HPV 1 x 10^7 pfu
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^9 vp and MVA-HPV 1 x 10^7 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Main Phase Group 2

Arm description:

Main Phase Group 2, ChAdOx1-HPV 2 x 10^10 vp on Day 0 and MVA-HPV 1 x 10^7 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV 2 x 10^10 vp and MVA-HPV 1 x 10^7 pfu
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^10 vp and MVA-HPV 1 x 10^7 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Main Phase Group 3

Arm description:

Main Phase Group 3, ChAdOx1-HPV 2 x 10^8 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV 2 x 10^8 vp and MVA-HPV 1 x 10^8 pfu
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^8 vp and MVA-HPV 1 x 10^8 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Main Phase Group 4

Arm description:

Main Phase Group 4, ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV 2 x 10^9 vp and MVA-HPV 1 x 10^8 pfu
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^9 vp and MVA-HPV 1 x 10^8 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Main Phase Group 5

Arm description:

Main Phase Group 5 ChAdOx1-HPV 2 x 10^10 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV 2 x 10^10 vp and MVA-HPV 1 x 10^8 pfu
Investigational medicinal product code	VTP-200
Other name	N/A
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^10 vp and MVA-HPV 1 x 10^8 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Main Phase Group 6

Arm description:

Placebo on Day 0 and Day 28

Arm type	Placebo
Investigational medicinal product name	1x 0.25mL placebo 0.9% saline injection at day 0 and 1x 0.5mL placebo injection at day 28
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

1x 0.25mL placebo 0.9% saline injection at day 0 and 1x 0.5mL placebo injection at day 28.
Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Lead-in Group A

Arm description:

ChAdOx1-HPV 2 x 10^8 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV and MVA-HPV
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^8 vp and MVA-HPV 1 x 10^7 pfu. Both doses were given by intramuscular injection into the deltoid muscle.

Arm title	Lead-in Group B

Arm description:

ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV and MVA-HPV
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^9 vp and MVA-HPV 1 x 10^7 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Arm title	Lead-in Group C

Arm description:

ChAdOx1-HPV 2 x 10^10 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28

Arm type	Experimental
Investigational medicinal product name	ChAdOx1-HPV and MVA-HPV
Investigational medicinal product code	VTP-200
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use, Injection

Dosage and administration details:

ChAdOx1-HPV 2 x 10^10 vpMVA-HPV 1 x 10^8 pfu. Both doses were given by intramuscular injection into the deltoid muscle

Number of subjects in period 1	Main Phase Group 1	Main Phase Group 2	Main Phase Group 3
Started	17	16	9
Completed	17	16	9
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Main Phase Group 4	Main Phase Group 5	Main Phase Group 6
Started	9	16	32
Completed	9	14	31
Not completed	0	2	1

Consent withdrawn by subject	-	1	-
Physician decision	-	-	1
Lost to follow-up	-	1	-

Number of subjects in period 1	Lead-in Group A	Lead-in Group B	Lead-in Group C
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Lost to follow-up	-	-	-

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	108	108	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Age at Consent (Years)			
Units: years			
median	36.5		
full range (min-max)	25 to 55	-	
Gender categorical Units: Subjects			
Female	108	108	
Male	0	0	
Is the Participant of Child-bearing Potential? Units: Subjects			
Yes	96	96	
No (post-menopausal)	10	10	
No (Surgically Sterile)	2	2	
No (Other)	0	0	
Ethnicity Units: Subjects			
Hispanic or Latino	5	5	
Not Hispanic or Latino	103	103	
Not Reported	0	0	
Unknown	0	0	
Race Units: Subjects			
American Indian/Alaska Native	1	1	
Asian	2	2	
Black/African American	0	0	
Native Hawaiian/Other Pacific Islander	0	0	

White	102	102	
Other (British Greek)	1	1	
Other (Mixed Other)	1	1	
Other (Mixed White Asian)	1	1	
Smoking History Units: Subjects			
Yes	37	37	
No	71	71	
History of Alcohol Abuse Units: Subjects			
Never	107	107	
Current	0	0	
Previous	1	1	
History of Illicit Drug Use Units: Subjects			
yes	3	3	
No	105	105	
Height (cm) at Screening Units: centimetre			
median	165.5		
full range (min-max)	152 to 187	-	
Weight (kg) at Screening Units: kilogram(s)			
median	68.25		
full range (min-max)	47.3 to 144.6	-	
BMI at Screening Units: kilogram(s)/square metre			
median	24.62		
full range (min-max)	17.4 to 49.5	-	

End points

End points reporting groups

Reporting group title	Main Phase Group 1
Reporting group description: Main Phase Group 1, ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28	
Reporting group title	Main Phase Group 2
Reporting group description: Main Phase Group 2, ChAdOx1-HPV 2 x 10^10 vp on Day 0 and MVA-HPV 1 x 10^7 pfu on Day 28	
Reporting group title	Main Phase Group 3
Reporting group description: Main Phase Group 3, ChAdOx1-HPV 2 x 10^8 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28	
Reporting group title	Main Phase Group 4
Reporting group description: Main Phase Group 4, ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28	
Reporting group title	Main Phase Group 5
Reporting group description: Main Phase Group 5 ChAdOx1-HPV 2 x 10^10 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28	
Reporting group title	Main Phase Group 6
Reporting group description: Placebo on Day 0 and Day 28	
Reporting group title	Lead-in Group A
Reporting group description: ChAdOx1-HPV 2 x 10^8 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28	
Reporting group title	Lead-in Group B
Reporting group description: ChAdOx1-HPV 2 x 10^9 vp on Day 0, and MVA-HPV 1 x 10^7 pfu on Day 28	
Reporting group title	Lead-in Group C
Reporting group description: ChAdOx1-HPV 2 x 10^10 vp on Day 0, and MVA-HPV 1 x 10^8 pfu on Day 28	
Subject analysis set title	Safety Analysis Set
Subject analysis set type	Safety analysis
Subject analysis set description: The Safety Analysis Set consists of all participants who received at least one dose of IP.	
Subject analysis set title	Intent to Treat Analysis set (pooled active)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Pooled Active ITT	
Subject analysis set title	Intent to Treat Analysis set (Placebo)
Subject analysis set type	Modified intention-to-treat
Subject analysis set description: ITT Placebo	
Subject analysis set title	IMM Analysis Set Pooled Active
Subject analysis set type	Sub-group analysis
Subject analysis set description: The immunogenicity (IMM) analysis set will consist of all participants in the per-protocol set who have available immunogenicity data (i.e., enrolled in the immunogenicity sub-study) to evaluate the immunogenicity endpoints and who do not have any protocol deviations that would Impact the immunology results.	
Subject analysis set title	IMM Analysis Set Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The immunogenicity (IMM) analysis set will consist of all participants in the per-protocol set who have available immunogenicity data (i.e., enrolled in the immunogenicity sub-study) to evaluate the immunogenicity endpoints and who do not have any protocol deviations that would impact the immunology results.

Primary: Safety and reactogenicity: incidence of adverse events (AEs), serious adverse events (SAEs), ≥Grade 3 VTP-200-related adverse events within 4 weeks of administration and adverse events leading to VTP-200 discontinuation

End point title	Safety and reactogenicity: incidence of adverse events (AEs), serious adverse events (SAEs), ≥Grade 3 VTP-200-related adverse events within 4 weeks of administration and adverse events leading to VTP-200 discontinuation[1]

End point description:

End point type	Primary

End point timeframe:

3 months for lead in phase, and 12 months for main phase

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: N/A this was not performed and not required

End point values	Safety Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	108			
Units: Incidence of AE's and SAE's				
Number of Reported Solicited Symptoms	369			
Number of Reported Adverse Events	216			
Number of TEAEs	205			
Participants Reporting Any Solicited Symptom or AE	105			
Solicited Symptoms	91			
Local symptoms	69			
Local symptoms Grade 3+	1			
Systemic symptoms	83			
Systemic symptoms Grade 3+	7			
Unsolicited TEAE	82			
Unsolicited TEAE Related	19			
Unsolicited TEAE Grade 3+	3			
Unsolicited TEAE Related Grade 3+	0			
Serious AE	2			
Vaccine related SAE	0			
Death	0			
Suspected, unexpected, serious adverse reaction	0			
Any Grade 3+ Laboratory Abnormality	0			
AE Resulting in Study Discontinuation	0			
AE Resulting in Vaccine Discontinuation	0			

Attachments (see zip file)	Summary of Solicited Symptoms and Adverse

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage clearance of hrHPV infection at 12 months

End point title	Percentage clearance of hrHPV infection at 12 months

End point description:

End point type	Secondary

End point timeframe:

12 months

End point values	Intent to Treat Analysis set (pooled active)	Intent to Treat Analysis set (Placebo)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67[2]	32[3]		
Units: % of participants meeting criteria				
Participants with detectable HPV DNA (Screening)	67	32		
Participants with detectable HPV DNA (M6)	51	24		
Participants with detectable HPV DNA (M12)	44	20		
Pts who are cleared of hrHPV at Month 6 (Yes)	14	6		
Pts who are cleared of hrHPV at Month 6 (No)	51	24		
Pts who are cleared of hrHPV at Month 12 (Yes)	20	10		
Pts who are cleared of hrHPV at Month 12 (No)	44	20		
M12 recurrence following HPV clearance at M6	3	1		

Notes:

[2] - Pooled active (main phase)

[3] - Placebo

Attachments (see zip file)	Table 14.2.1.1.1 ITT Analysis Set/T_14_2_1_1_1.rtf

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of cervical lesions cleared as determined by colposcopy

End point title	Percentage of cervical lesions cleared as determined by colposcopy

End point description:

End point type	Secondary

End point timeframe:

12 Months

End point values	Intent to Treat Analysis set (pooled active)	Intent to Treat Analysis set (Placebo)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67[4]	32[5]		
Units: % of participants meeting criteria				
Transformation Zone Seen Screening and M6	35	14		
Transformation Zone Seen Screening and M12	53	25		
Clearance of Cervical Lesions Month 6	13	8		
Clearance of Cervical Lesions Month 12	26	10		

Notes:

[4] - Pooled active (main phase)

[5] - Placebo

Attachments (see zip file)	Table 14.2.2.1 ITT analysis set/T_14_2_2_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Individual phenotypic subsets of CD4+ and CD8+ T cells induced by VTP-200

End point title	Individual phenotypic subsets of CD4+ and CD8+ T cells induced by VTP-200

End point description:

Data is presented for participants with available ICS data at each of the timepoints

End point type	Other pre-specified

End point timeframe:

12 months

End point values	IMM Analysis Set Pooled Active	IMM Analysis Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[6]	19[7]		
Units: Observed median				
median (confidence interval 95%)				
CD4+ 50JS Baseline	0.003 (0.000 to 0.009)	0.009 (0.000 to 0.022)		
CD4+ 50JS Day 28	0.009 (0.004 to 0.014)	0.006 (0.000 to 0.017)		
CD4+ 50JS Day 35	0.034 (0.024 to 0.065)	0.000 (0.000 to 0.005)		

CD4+ 50JS Month 3	0.022 (0.013 to 0.037)	0.007 (0.000 to 0.012)		
CD4+ 50JS Month 12	0.024 (0.014 to 0.030)	0.000 (0.000 to 0.005)		
CD4+ 130HS Baseline	0.008 (0.005 to 0.014)	0.007 (0.000 to 0.013)		
CD4+ 130HS Day 28	0.014 (0.008 to 0.020)	0.006 (0.000 to 0.016)		
CD4+ 130HS Day 35	0.046 (0.027 to 0.063)	0.000 (0.000 to 0.006)		
CD4+ 130HS Month 3	0.026 (0.017 to 0.037)	0.001 (0.000 to 0.013)		
CD4+ 130HS Month 12	0.019 (0.010 to 0.035)	0.001 (0.000 to 0.007)		
CD4+ (130HS + 50JS) Baseline	0.014 (0.008 to 0.018)	0.018 (0.001 to 0.032)		
CD4+ (130HS + 50JS) Day 28	0.026 (0.014 to 0.035)	0.013 (0.000 to 0.035)		
CD4+ (130HS + 50JS) Day 35	0.087 (0.054 to 0.141)	0.000 (0.000 to 0.006)		
CD4+ (130HS + 50JS) Month 3	0.052 (0.025 to 0.074)	0.008 (0.000 to 0.026)		
CD4+ (130HS + 50JS) Month 12	0.043 (0.023 to 0.071)	0.001 (0.000 to 0.010)		
CD8+ 50JS Baseline	0.000 (0.000 to 0.028)	0.020 (0.000 to 0.060)		
CD8+ 50JS Day 28	0.030 (0.011 to 0.058)	0.005 (0.000 to 0.014)		
CD8+ 50JS Day 35	0.106 (0.055 to 0.206)	0.014 (0.000 to 0.037)		
CD8+ 50JS Month 3	0.044 (0.025 to 0.082)	0.023 (0.000 to 0.047)		
CD8+ 50JS Month 12	0.047 (0.027 to 0.080)	0.004 (0.000 to 0.030)		
CD8+ 130HS Baseline	0.003 (0.000 to 0.033)	0.010 (0.000 to 0.031)		
CD8+ 130HS Day 28	0.023 (0.009 to 0.050)	0.007 (0.000 to 0.044)		
CD8+ 130HS Day 35	0.087 (0.055 to 0.127)	0.006 (0.000 to 0.027)		
CD8+ 130HS Month 3	0.046 (0.019 to 0.082)	0.028 (0.000 to 0.077)		
CD8+ 130HS Month 12	0.027 (0.007 to 0.046)	0.013 (0.000 to 0.039)		
CD8+ (130HS + 50JS) Baseline	0.003 (0.000 to 0.044)	0.043 (0.000 to 0.076)		
CD8+ (130HS + 50JS) Day 28	0.081 (0.016 to 0.117)	0.017 (0.000 to 0.037)		
CD8+ (130HS + 50JS) Day 35	0.261 (0.126 to 0.443)	0.036 (0.000 to 0.058)		
CD8+ (130HS + 50JS) Month 3	0.092 (0.062 to 0.198)	0.030 (0.000 to 0.134)		
CD8+ (130HS + 50JS) Month 12	0.073 (0.036 to 0.128)	0.020 (0.000 to 0.050)		

Notes:

[6] - Observed median data are presented only for participants with available data at each timepoint.

[7] - Observed median data are presented only for participants with available data at each timepoint.

Attachments (see zip file)	Table 14.2.4.1 IMM analysis set/T_14_2_4_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Individual phenotypic subsets of CD4+ and CD8+ T cells induced by VTP-200

End point title	Individual phenotypic subsets of CD4+ and CD8+ T cells induced by VTP-200

End point description:

Change from baseline data are only presented for participants with available date at each of the timepoints.

End point type	Other pre-specified

End point timeframe:

12 months

End point values	IMM Analysis Set Pooled Active	IMM Analysis Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[8]	19[9]		
Units: Median Percentage change from baseline				
median (confidence interval 95%)				
CD4+ 50JS Day 28	0.005 (0.000 to 0.010)	-0.001 (-0.014 to 0.000)		
CD4+ 50JS Day 35	0.025 (0.016 to 0.057)	-0.006 (-0.009 to 0.000)		
CD4+ 50JS Month 3	0.015 (0.002 to 0.030)	0.000 (-0.022 to 0.002)		
CD4+ 50JS Month 12	0.015 (0.012 to 0.027)	-0.009 (-0.017 to 0.000)		
CD4+ 130HS Day 28	0.002 (-0.001 to 0.012)	0.000 (-0.004 to 0.006)		
CD4+ 130HS Day 35	0.030 (0.007 to 0.055)	0.000 (-0.004 to 0.000)		
CD4+ 130HS Month 3	0.012 (0.005 to 0.023)	-0.001 (-0.005 to 0.002)		
CD4+ 130HS Month 12	0.011 (0.000 to 0.025)	-0.003 (-0.011 to 0.002)		
CD4+ (130HS + 50JS) Day 28	0.009 (0.000 to 0.019)	-0.000 (-0.016 to 0.010)		
CD4+ (130HS + 50JS) Day 35	0.058 (0.029 to 0.099)	-0.001 (-0.016 to 0.000)		
CD4+ (130HS + 50JS) Month 3	0.026 (0.017 to 0.043)	-0.001 (-0.023 to 0.003)		
CD4+ (130HS + 50JS) Month 12	0.025 (0.011 to 0.056)	-0.016 (-0.027 to 0.002)		
CD8+ 50JS Day 28	0.006 (0.000 to 0.023)	-0.001 (-0.040 to 0.005)		
CD8+ 50JS Day 35	0.075 (0.037 to 0.144)	0.000 (-0.024 to 0.028)		
CD8+ 50JS Month 3	0.032 (0.004 to 0.053)	-0.001 (-0.040 to 0.000)		
CD8+ 50JS Month 12	0.033 (0.000 to 0.063)	-0.001 (-0.032 to 0.000)		

CD8+ 130HS Day 28	0.003 (0.000 to 0.015)	0.000 (-0.019 to 0.030)		
CD8+ 130HS Day 35	0.045 (0.021 to 0.109)	0.000 (-0.015 to 0.006)		
CD8+ 130HS Month 3	0.015 (0.006 to 0.028)	0.003 (0.000 to 0.047)		
CD8+ 130HS Month 12	0.000 (0.000 to 0.027)	0.000 (-0.027 to 0.021)		
CD8+ (130HS + 50JS) Day 28	0.002 (0.000 to 0.064)	-0.005 (-0.036 to 0.006)		
CD8+ (130HS + 50JS) Day 35	0.131 (0.073 to 0.327)	-0.009 (-0.052 to 0.034)		
CD8+ (130HS + 50JS) Month 3	0.056 (0.025 to 0.083)	0.000 (-0.053 to 0.067)		
CD8+ (130HS + 50JS) Month 12	0.034 (0.000 to 0.078)	-0.003 (-0.085 to 0.000)		

Notes:

[8] - Change from baseline data are presented for participants that have available data at each timepoint
[9] - Change from baseline data are presented for participants that have available data at each timepoint

Attachments (see zip file)	Table 14.2.4.1 IMM analysis set/T_14_2_4_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: The T cell breadth of response to the components of VTP-200

End point title	The T cell breadth of response to the components of VTP-200

End point description:

Median observed data are presented for participants with available data at each timepoint.
DMSO-subtracted antigen-specific IFN-γ ELISpot response (SFU – background/106 PBMC)- Pooled Active Group vs Placebo
IMM Analysis Set

End point type	Other pre-specified

End point timeframe:

12 months

End point values	IMM Analysis Set Pooled Active	IMM Analysis Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[10]	19[11]		
Units: Observed median				
median (confidence interval 95%)				
E1 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E1 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E1 Day 35	61.5 (0.0 to 169.0)	0.0 (0.0 to 0.0)		
E1 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E1 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		

E2 Day 35	101.0 (60.0 to 202.0)	0.0 (0.0 to 0.0)		
E2 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Day 35	137.5 (70.0 to 237.0)	0.0 (0.0 to 0.0)		
E6 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Junction Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Junction Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Junction Day 35	349.5 (202.0 to 638.0)	0.0 (0.0 to 0.0)		
Junction Month 3	86.5 (0.0 to 130.0)	0.0 (0.0 to 0.0)		
Junction Month 12	0.0 (0.0 to 67.0)	0.0 (0.0 to 0.0)		
Total ELISpot Baseline	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Total ELISpot Day 28	0.0 (0.0 to 125.0)	0.0 (0.0 to 0.0)		
Total ELISpot Day 35	889.0 (490.0 to 1469.0)	0.0 (0.0 to 0.0)		
Total ELISpot Month 3	103.5 (0.0 to 210.0)	0.0 (0.0 to 0.0)		
Total ELISpot Month 12	0.0 (0.0 to 142.0)	0.0 (0.0 to 0.0)		

Notes:

[10] - Data is only presented for participants with data available at each timepoint

[11] - Data is only presented for participants with data available at each timepoint

Attachments (see zip file)	Table 14.2.5.1 IMM analysis set/T_14_2_5_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: The T cell breadth of response to the components of VTP-200

End point title	The T cell breadth of response to the components of VTP-200

End point description:

DMSO-subtracted antigen-specific IFN-γ ELISpot response (SFU – background/106 PBMC)- Pooled Active Group vs Placebo
IMM Analysis Set
Results are presented for participants with available data at each of the timepoints

End point type	Other pre-specified

End point timeframe:

12 months

End point values	IMM Analysis Set Pooled Active	IMM Analysis Set Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	54[12]	19[13]		
Units: Median change from baseline				
median (confidence interval 95%)				
E1 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E1 Day 35	61.5 (0.0 to 169.0)	0.0 (0.0 to 0.0)		
E1 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E1 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Day 35	101.0 (60.0 to 202.0)	0.0 (0.0 to 0.0)		
E2 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E2 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E4 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E5 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Day 35	137.5 (70.0 to 237.0)	0.0 (0.0 to 0.0)		
E6 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E6 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Day 35	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Month 3	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
E7 Month 12	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Junction Day 28	0.0 (0.0 to 0.0)	0.0 (0.0 to 0.0)		
Junction Day 35	349.5 (202.0 to 638.0)	0.0 (0.0 to 0.0)		
Junction Month 3	76.5 (0.0 to 130.0)	0.0 (0.0 to 0.0)		
Junction Month 12	0.0 (0.0 to 67.0)	0.0 (0.0 to 0.0)		
Total ELISpot Day 28	0.0 (0.0 to 88.0)	0.0 (0.0 to 0.0)		

Total ELISpot Day 35	889.0 (490.0 to 1469.0)	0.0 (0.0 to 0.0)		
Total ELISpot Month 3	96.5 (0.0 to 210.0)	0.0 (0.0 to 0.0)		
Total ELISpot Month 12	0.0 (0.0 to 90.0)	0.0 (0.0 to 0.0)		

Notes:

[12] - data is presented for participants that have available data at each timepoint

[13] - data is presented for participants that have available data at each timepoint

Attachments (see zip file)	Table 14.2.4.1 IMM analysis set/T_14_2_5_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Cervical lesion size compared to baseline, if measured

End point title	Cervical lesion size compared to baseline, if measured

End point description:

Cervical Lesion Size and Change from Baseline
ITT Analysis Set
Data are presented for participants with available data at each timepoint

End point type	Other pre-specified

End point timeframe:

12 months

End point values	Intent to Treat Analysis set (pooled active)	Intent to Treat Analysis set (Placebo)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67[14]	32[15]		
Units: % of participants meeting criteria				
Pt's with primary lesion still present at M6	22	5		
Primary Lesion Size Changed at Month 6 (Smaller)	12	3		
Primary Lesion Size Changed at Month 6 (Larger)	3	0		
Primary Lesion Size Changed at Month 6 (no change)	6	1		
Pt's with primary lesion still present at M12	22	8		
Primary Lesion Size Changed at Month 12 (Smaller)	10	4		
Primary Lesion Size Changed at Month 12 (Larger)	1	1		
Primary Lesion Size Changed at Month 12 (No change	9	1		

Notes:

[14] - Data are presented for participants with available data at each timepoint

[15] - Data are presented for participants with available data at each timepoint

Attachments (see zip file)	Table 14.2.3.1 ITT analysis set/T_14_2_3_1.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Genotype and rate of clearance of HPV, HPV Genotype at Screening: Presence of HPV 16 and/or HPV 18

End point title	Genotype and rate of clearance of HPV, HPV Genotype at Screening: Presence of HPV 16 and/or HPV 18

End point description:

Proportion of Clearance of hrHPV Infection by HPV Genotype - Pooled Active Group vs Placebo
ITT Analysis Set
Data are presented for participants with available data at each of the timepoints
HPV Gynotype at Screening: Presence of HPV 16 and/or HPV 18

End point type	Other pre-specified

End point timeframe:

12 months

End point values	Intent to Treat Analysis set (pooled active)	Intent to Treat Analysis set (Placebo)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	19[16]	16[17]		
Units: % of participants meeting criteria				
Participants with detectable HPV DNA (Screening)	19	16		
Participants with detectable HPV DNA (Month 6)	17	12		
Participants with detectable HPV DNA (Month 12)	16	14		
Participants cleared of hrHPV at M6 (Yes)	2	2		
Participants cleared of hrHPV at M6 (No)	17	12		
Participants cleared of hrHPV at M12 (Yes)	3	1		
Participants cleared of hrHPV at M12 (No)	16	14		
M12 recurrence following HPV clearance at M6	1	1		

Notes:

[16] - Data are presented for participants with available data at each timepoint

[17] - Data are presented for participants with available data at each timepoint

Attachments (see zip file)	Table 14.2.1.7 ITT Analysis set/T_14_2_1_7.rtf

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Genotype and rate of clearance of HPV,HPV Genotype at Screening: All other genotypes except HPV 16 and HPV 18

End point title	Genotype and rate of clearance of HPV,HPV Genotype at Screening: All other genotypes except HPV 16 and HPV 18

End point description:

Proportion of Clearance of hrHPV Infection by HPV Genotype - Pooled Active Group vs Placebo
ITT Analysis Set
Data are presented for participants with available data at each timepoint
HPV Genotype at Screening: All other genotypes except HPV 16 and HPV 18

End point type	Other pre-specified

End point timeframe:

12 months

End point values	Intent to Treat Analysis set (pooled active)	Intent to Treat Analysis set (Placebo)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48[18]	16[19]		
Units: % of participants meeting criteria				
Participants with detectable HPV DNA (Screening)	48	16		
Participants with detectable HPV DNA (Month 6)	34	12		
Participants with detectable HPV DNA (Month 12)	28	6		
Pt's who are cleared of hrHPV at Month 6 (Yes)	12	4		
Pt's who are cleared of hrHPV at Month 6 (No)	34	12		
Pt's who are cleared of hrHPV at Month 12 (Yes)	17	9		
Pt's who are cleared of hrHPV at Month 12 (No)	28	6		
M12 recurrence following HPV clearance at M6	2	0		

Notes:

[18] - Data are presented for participants with available data at each timepoint

[19] - Data are presented for participants with available data at each timepoint

Attachments (see zip file)	Table 14.2.1.7 ITT Analysis set/T_14_2_1_7.rtf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The reporting period for adverse events began on the date the informed consent was signed until Month 3 for the lead-in phase and 12 months for the main phase	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Overall Trial
Reporting group description:	
Safety Analysis Set	

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 108 (1.85%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Immune system disorders			
Cholelithiasis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Schizophrenia			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	82 / 108 (75.93%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Basal cell carcinoma, Fibroadenoma of breast			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Vascular disorders			
Hypertension, Hypotension			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chills, Drug withdrawal syndrome, Fatigue, Influenza like illness, Injection site bruising	Additional description: Injection site pain, Non-cardiac chest pain, Pyrexia, Vaccination site pain, Vaccination site paraesthesia		
subjects affected / exposed	12 / 108 (11.11%)		
occurrences (all)	15		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Cervical polyp, Coital bleeding, Dysmenorrhoea, Dyspareunia, Endometriosis, Hypomenorrhoea,	Additional description: Menorrhagia, Metrorrhagia, Uterine spasm, Vaginal discharge, Vaginal haemorrhage, Vaginal ulceration		
subjects affected / exposed	11 / 108 (10.19%)		
occurrences (all)	15		
Respiratory, thoracic and mediastinal disorders			
Cough, Nasal polyps, Oropharyngeal pain, Pharyngeal disorder, Rhinorrhoea			
subjects affected / exposed	9 / 108 (8.33%)		
occurrences (all)	12		
Psychiatric disorders			
Depression, Schizophrenia			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Investigations			
Blood cholesterol increased, Body temperature increased			
subjects affected / exposed	2 / 108 (1.85%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			

Fall, Foot fracture, Ligament sprain, Procedural dizziness, Radius fracture, Road traffic accident,	Additional description: Traumatic fracture, Vaccination complication		
subjects affected / exposed	8 / 108 (7.41%)		
occurrences (all)	8		
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	2		
Nervous system disorders			
Dizziness, Headache, Hypoaesthesia, Migraine, Neuralgia, Paraesthesia, Sciatica			
subjects affected / exposed	20 / 108 (18.52%)		
occurrences (all)	27		
Blood and lymphatic system disorders			
Anaemia, Lymphadenopathy			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences (all)	4		
Gastrointestinal disorders			
Abdominal Pain Lower, Abdominal pain upper, Aphthous ulcer, Diarrhoea, Dyspepsia, Gingival bleeding	Additional description: Haemorrhoids, Irritable bowel syndrome, Nausea, Proctalgia, Toothache, Vomiting		
subjects affected / exposed	17 / 108 (15.74%)		
occurrences (all)	20		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia, Pruritus, Psoriasis, Urticaria			
subjects affected / exposed	4 / 108 (3.70%)		
occurrences (all)	5		
Musculoskeletal and connective tissue disorders			
Arthralgia, back pain, Joint swelling, Musculoskeletal stiffness, Myalgia, Neck pain	Additional description: Plantar fasciitis, Tendonitis		
subjects affected / exposed	12 / 108 (11.11%)		
occurrences (all)	13		
Infections and infestations			

Asymptomatic COVID-19, Bacterial vaginosis, COVID-19, Cystitis, Cytomegalovirus infection	Additional description: Gastroenteritis viral, Herpes zoster, Influenza, Labyrinthitis, Laryngitis, Lower respiratory tract infection, Nasopharyngitis, Otitis externa, Paronychia, Rhinitis, Sinusitis, Tonsillitis, Upper respiratory tract infection, Urinary tract infection		
subjects affected / exposed	55 / 108 (50.93%)		
occurrences (all)	80		
Viral infection			
subjects affected / exposed	3 / 108 (2.78%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Insulin resistance			
subjects affected / exposed	1 / 108 (0.93%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2020	Protocol v2.0: Changes were made to: • Align the documentation of persistent hrHPV infection inclusion criteria with clinical practice in the secondary care setting • Remove reference to focal CIN2 to align with standard of care in all countries in which the study is to be performed. Consequently, Pap smears will no longer be performed. • Update the target concentration of ChAdOx1-HPV to 8 x 1010 vp/mL as the drug product manufacture yield exceeded expectations. The delivered doses to the participants remain the same by use of a different injected volume. • Update the Investigational Medicinal Product (IMP) storage conditions to 2-8°C, as a result of recently reported stability data • Allow for sites to take only one cytobrush sample. Collection and analysis of a second sample will be performed only by those sites who can ensure delivery of a sample to the analytical laboratory within a 2-hour window from the sample being taken. • Mandate that the Investigator should notify the Sponsor within 24 hours of becoming aware of an SAE and clarify that SAEs should be reported via the SAE page of the eCRF • Ensure that colposcopy data collected is appropriate to the development of the study vaccines • Provide further clarity and correct typographical errors
29 May 2020	In response to Medicines & Healthcare products Regulatory Agency (MHRA), UK assessment: • Clarification of the data to be reviewed by the SMC to support dose escalation between the groups has been added. • Clarification that review of the safety profile results and adverse events of the sentinel participant 72 hours after dosing in each group in the lead-in phase will be performed by the CRO Medical Monitor and a review memo will be sent to each of the sites participating in the lead-in phase to confirm that the 2nd and 3rd participant may be dosed has been added. • The dose of MVA-HPV administered to participants in Group C of the lead-in phase has been amended to 1 x 108pfu. • The study stopping/pausing rules have been updated to include two Grade 3 unsolicited adverse events occur that are considered related to study vaccine, regardless of type • The definition of post-menopausal status has been updated. • Clarification of the duration of contraception requirements has been added. In response to Federal Agency for Medicines and Health Products (FAMHP), Belgium assessment: • Clarification of the data to be reviewed by the SMC to support dose escalation between the groups and clarification that the dosing of a sentinel participant in the lead-in phase applies at both Day 0 and Day 28 has been added. • The dose of MVA-HPV administered to participants in Group C of the lead-in phase has been amended to 1 x 108pfu. • Clarification that progestogen-only hormonal contraceptives without inhibition of ovulation are not considered to be highly effective, has been added Clarification that the presence of blood dyscrasias will exclude a potential participant from the study. • The study stopping/pausing rules have been updated to include one Grade 3 adverse event considered related to the study vaccine, regardless of type, during the lead-in phase.

04 August 2020	Changes were made to: • Update the study vaccine storage conditions to below -65°C to allow for a longer storage duration at investigator sites. Clarify the temperature record review process upon study vaccine shipment and clarify that additional study vaccine administration guidance is contained in the Pharmacy Manual. • Introduce individual participant stopping criteria to improve participant safety. • Introduce SARS-CoV-2 PCR testing at screening and prior to Day 0 and Day 28, if the participant is showing symptoms of COVID-19, or there has been known exposure, to improve participant safety. • Add an exclusion criterion of 'Current infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as evidenced by PCR laboratory testing' to improve participant safety. • Amend exclusion criterion 2 to align with the prednisone dose included in the list of concomitant medication to be avoided in Section 5.10
25 June 2021	Changes were made to: • Update the Sponsor's Authorised Representative to Margaret Marshall MD • Update the summary of clinical experience to reflect use of the ChAdOx1-vectored COVID-19 vaccine and Vaccitech access to study data • Update the study vaccine storage conditions to below -70°C to reflect current stability data. • Remove study-specific SARS-CoV-2 PCR testing to improve site staff and participant safety. Sites will follow their local SARS-CoV-2 public health guidance and procedures. • Amend inclusion criterion 4 to recognize sexual abstinence as an acceptable method of birth control only if the participant refrains from heterosexual intercourse during the entire study period and it is the usual lifestyle of the participant, in order to make it consistent with Heads of Medicines Agencies (HMA), Clinical Trials Facilitation Group (CTFG) guidance. • Amend exclusion criterion 5 to add an example of possible previous severe allergen. • Amend exclusion criterion 7 and Section 5.10 to reflect current known ChAdOx1 vaccine potential interactions. • Allow for study vaccinations to be administered within a window of ± 2 days • Reformat the study pausing/stopping rules to clarify meaning. • Add the solicited adverse event severity rating guidance provided to the participants. • Add a Belgium Co-ordinating Principal Investigator to the Safety Monitoring Committee

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported