Clinical trial results:
Double-Blind, Randomized, Placebo-Controlled Phase 2b, Multi-center Study to Evaluate the Safety, Tolerability, Efficacy and Immunogenicity of a 2-Dose and a 3- Dose Regimen of V160 (Cytomegalovirus [CMV] Vaccine) in Healthy Seronegative Women, 16 to 35 Years of Age

Summary

EudraCT number	2017-004233-86
Trial protocol	FI ES
Global end of trial date	30 June 2021

Results information

Result version number	v1 (current)
This version publication date	17 November 2021
First version publication date	17 November 2021

Trial information

Trial identification

Sponsor protocol code	V160-002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03486834
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	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	30 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 October 2020
Global end of trial reached?	Yes
Global end of trial date	30 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety, tolerability, and efficacy of the cytomegalovirus (CMV) vaccine (V160) administered in a 2-dose or 3-dose regimen to healthy seronegative women 16 to 35 years of age. Participants received blinded V160 on Day 1, Month 2, and Month 6 (3-dose regimen), V160 on Day 1 and Month 6 and placebo at Month 2 (2-dose regimen), or placebo on Day 1, Month 2, and Month 6, and were followed to approximately Month 24. The primary hypothesis of the study was that administration of a 3-dose regimen of V160 will reduce the incidence of primary CMV infection compared to placebo.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 58
Country: Number of subjects enrolled	Canada: 316
Country: Number of subjects enrolled	Spain: 164
Country: Number of subjects enrolled	Finland: 400
Country: Number of subjects enrolled	Israel: 260
Country: Number of subjects enrolled	Russian Federation: 75
Country: Number of subjects enrolled	United States: 927
Worldwide total number of subjects	2200
EEA total number of subjects	564

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)	53
Adults (18-64 years)	2147
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of approximately 2100 participants were planned to be enrolled with 2200 participants actually randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V160 3-Dose Regimen

Arm description:

Participants received V160 vaccination by intramuscular (IM) injection on Day 1, Month 2, and Month 6.

Arm type	Experimental
Investigational medicinal product name	V160
Investigational medicinal product code	
Other name	Human cytomegalovirus vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

V160 was administered as a 0.5 mL (100 Units/0.5 mL dose with Merck aluminum phosphate adjuvant [MAPA], 4°C stable formulation) IM injection.

Arm title	V160 2-Dose Regimen

Arm description:

Participants received V160 vaccination by IM injection on Day 1 and Month 6 and placebo at Month 2.

Arm type	Experimental
Investigational medicinal product name	V160
Investigational medicinal product code	
Other name	Human cytomegalovirus vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

V160 was administered as a 0.5 mL (100 Units/0.5 mL dose with Merck aluminum phosphate adjuvant [MAPA], 4°C stable formulation) IM injection.

Arm title	Placebo

Arm description:

Participants received placebo by IM injection on Day 1, Month 2, and Month 6.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:
Saline solution administered as a 0.5 mL IM injection

Number of subjects in period 1	V160 3-Dose Regimen	V160 2-Dose Regimen	Placebo
Started	733	733	734
Treatment 1	729	729	733
Treatment 2	680	680	679
Treatment 3	614	631	622
Completed	614	631	622
Not completed	119	102	112
Consent withdrawn by subject	46	46	52
Non-compliance with Study Drug	2	2	-
Physician decision	5	2	3
Adverse event, non-fatal	8	7	-
Protocol Deviation	2	3	3
Randomized but not treated	4	4	1
Pregnancy	10	12	12
Withdrawal by Parent/Guardian	1	2	2
Lost to follow-up	41	24	39

Baseline characteristics

Reporting groups	
Reporting group title	V160 3-Dose Regimen
Reporting group description:	
Participants received V160 vaccination by intramuscular (IM) injection on Day 1, Month 2, and Month 6.	
Reporting group title	V160 2-Dose Regimen
Reporting group description:	
Participants received V160 vaccination by IM injection on Day 1 and Month 6 and placebo at Month 2.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo by IM injection on Day 1, Month 2, and Month 6.	

Reporting group values	V160 3-Dose Regimen	V160 2-Dose Regimen	Placebo
Number of subjects	733	733	734
Age categorical Units: Particpants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	16	15	22
Adults (18-64 years)	717	718	712
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	26.0	26.1	25.9
standard deviation	± 5.0	± 4.9	± 4.9
Sex: Female, Male Units: Particpants			
Female	733	733	734
Male	0	0	0
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	1	4
Asian	6	7	6
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	47	49	43
White	657	652	665
More than one race	23	23	16
Unknown or Not Reported	0	1	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	144	145	143

Not Hispanic or Latino	588	585	587
Unknown or Not Reported	1	3	4

Reporting group values	Total		
Number of subjects	2200		
Age categorical Units: Particpants			
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)	53		
Adults (18-64 years)	2147		
From 65-84 years	0		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Particpants			
Female	2200		
Male	0		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	5		
Asian	19		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	139		
White	1974		
More than one race	62		
Unknown or Not Reported	1		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	432		
Not Hispanic or Latino	1760		
Unknown or Not Reported	8		

End points

End points reporting groups

Reporting group title	V160 3-Dose Regimen
Reporting group description:	
Participants received V160 vaccination by intramuscular (IM) injection on Day 1, Month 2, and Month 6.	
Reporting group title	V160 2-Dose Regimen
Reporting group description:	
Participants received V160 vaccination by IM injection on Day 1 and Month 6 and placebo at Month 2.	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo by IM injection on Day 1, Month 2, and Month 6.	

Primary: Number of Participants Who Became Infected With Wild-Type Cytomegalovirus Infection (CMVi) Starting at 4 Weeks Post Last Dose (V160 3-dose Regimen Group and Placebo Group)

End point title	Number of Participants Who Became Infected With Wild-Type Cytomegalovirus Infection (CMVi) Starting at 4 Weeks Post Last Dose (V160 3-dose Regimen Group and Placebo Group)[1]

End point description:

CMVi was defined as the detection of wild-type CMV (non vaccine type) by polymerase chain reaction in a single saliva or urine sample in a previously CMV-uninfected participant. CMVi cases in the 3-dose regimen and placebo groups were reported and incidence rate (per 100 person-years) calculated based on follow-up time starting at 4 weeks post last dose (Month 7) through approximately Month 24 (or time point to reach required cases for assessment). The percent reduction in CMVi incidence rate in the 3-dose regimen group compared to the placebo group was assessed. Participants who were CMV seronegative at Day 1 and CMV negative by polymerase chain reaction (PCR) for nonvaccine strain virus from post Day 1 through Month 7, had received all 3 injections/vaccinations within the vaccination visit window, and did not have any deviations from protocol deemed to potentially interfere with the evaluation of efficacy or immune response to injection of V160.

End point type	Primary

End point timeframe:

4 weeks post last vaccination (Month 7) up to ~Month 24

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: For this endpoint, V160 3-Dose regimen group and the placebo group were the only two arms being evaluated.

End point values	V160 3-Dose Regimen	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	543		
Units: Participants	14	24		

Statistical analyses

Statistical analysis title	Incidence Rate Estimate of V160 3-Dose
Comparison groups	V160 3-Dose Regimen v Placebo

Number of subjects included in analysis	1099
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence Rate Estimate
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	4.9

Statistical analysis title	Vaccine Efficacy V160 3-Dose Regimen
Comparison groups	V160 3-Dose Regimen v Placebo
Number of subjects included in analysis	1099
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Vaccine Efficacy
Point estimate	42.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.5
upper limit	71.1

Statistical analysis title	Incidence Rate Estimate of Placebo
Comparison groups	Placebo v V160 3-Dose Regimen
Number of subjects included in analysis	1099
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence Rate Estimate
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	7.6

Primary: Number of Participants With Solicited Injection-site Adverse Events

End point title	Number of Participants With Solicited Injection-site Adverse Events

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. Following

vaccination with V160 or placebo, the number of participants with solicited injection-site AEs was assessed. The analysis population included all randomized participants who received at least 1 injection of V160 or placebo, had safety follow-up data, and had been assigned to the treatment arm corresponding to the actual clinical material received.

End point type	Primary
End point timeframe:	
Up to 5 days after each vaccination	

End point values	V160 3-Dose Regimen	V160 2-Dose Regimen	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	728	729	732	
Units: Participants	683	668	249	

Statistical analyses

Statistical analysis title	V160 3-dose vs. Placebo
Comparison groups	V160 3-Dose Regimen v Placebo
Number of subjects included in analysis	1460
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	59.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	55.8
upper limit	63.5

Statistical analysis title	V160 2-dose vs. Placebo
Comparison groups	V160 2-Dose Regimen v Placebo
Number of subjects included in analysis	1461
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	57.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.5
upper limit	61.5

Primary: Number of Participants With Solicited Systemic AEs

End point title	Number of Participants With Solicited Systemic AEs

End point description:

An AE is any untoward medical occurrence in a participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. Following vaccination with V160 or placebo, the number of participants with solicited systemic AEs was assessed. The analysis population included all randomized participants who received at least 1 injection of V160 or placebo, had safety follow-up data, and had been assigned to the treatment arm corresponding to the actual clinical material received.

End point type	Primary

End point timeframe:

Up to 14 days after each vaccination

End point values	V160 3-Dose Regimen	V160 2-Dose Regimen	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	728	729	732	
Units: Participants	621	633	508	

Statistical analyses

Statistical analysis title	V160 3-dose vs.Placebo
Comparison groups	V160 3-Dose Regimen v Placebo
Number of subjects included in analysis	1460
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	15.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	11.7
upper limit	20.1

Statistical analysis title	V160 2-dose vs. Placebo
Comparison groups	V160 2-Dose Regimen v Placebo
Number of subjects included in analysis	1461
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	17.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.3
upper limit	21.6

Primary: Number of Participants With Vaccine-related Serious Adverse Events

End point title	Number of Participants With Vaccine-related Serious Adverse Events

End point description:

A serious adverse event (SAE) is an AE that is life-threatening, requires or prolongs an existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, or is another important medical event deemed such by medical or scientific judgment. Relatedness of an SAE to the study vaccine was determined by the investigator. Following vaccination with V160 or placebo, the number of participants with vaccine-related serious adverse events was assessed. The analysis population included all randomized participants who received at least 1 injection of V160 or placebo, had safety follow-up data, and had been assigned to the treatment arm corresponding to the actual clinical material received.

End point type	Primary

End point timeframe:

Up to 14 days after each vaccination

End point values	V160 3-Dose Regimen	V160 2-Dose Regimen	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	728	729	732	
Units: Participants	0	0	0	

Statistical analyses

Statistical analysis title	V160 3-dose vs. Placebo
Comparison groups	V160 3-Dose Regimen v Placebo
Number of subjects included in analysis	1460
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5

Statistical analysis title	V160 2-dose vs. Placebo

Comparison groups	V160 2-Dose Regimen v Placebo
Number of subjects included in analysis	1461
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in Percent
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	0.5

Secondary: Number of Participants Who Became Infected With Wild-Type CMV Infection Starting at 4 Weeks Post Last Dose (V160 2-dose Regimen Group and Placebo Group)

End point title	Number of Participants Who Became Infected With Wild-Type CMV Infection Starting at 4 Weeks Post Last Dose (V160 2-dose Regimen Group and Placebo Group)[2]

End point description:

CMVi is defined as detection of wild-type CMV (non-vaccine type) by polymerase chain reaction in a single saliva or urine sample in a previously CMV-uninfected participant. CMVi cases in the 2-dose regimen and placebo groups were reported and incidence rate (per 100 person-years) calculated based on follow-up time starting at 4 weeks post last dose (Month 7) through approximately Month 24 (or time point to reach required cases for assessment). The percent reduction in CMVi incidence rate in the 2-dose regimen group compared to the placebo group was assessed. The analysis population included participants who were CMV seronegative at Day 1 and CMV negative by polymerase chain reaction (PCR) for nonvaccine strain virus from post Day 1 through Month 7, had received all 2 injections/vaccinations within the vaccination visit window, and did not have any deviations from protocol deemed to potentially interfere with the evaluation of efficacy or immune response to injection of V160.

End point type	Secondary

End point timeframe:

4 weeks post last vaccination (Month 7) up to ~Month 24

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: For this endpoint, V160 2-Dose regimen group and the placebo group were the only two arms being evaluated.

End point values	V160 2-Dose Regimen	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	546	543		
Units: Participants	31	24		

Statistical analyses

Statistical analysis title	Incidence Rate Estimate V160 2-Dose
Comparison groups	V160 2-Dose Regimen v Placebo

Number of subjects included in analysis	1089
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence Rate Estimate
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.6
upper limit	9.5

Statistical analysis title	Incidence Rate Estimate Placebo
Comparison groups	Placebo v V160 2-Dose Regimen
Number of subjects included in analysis	1089
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Incidence Rate Estimate
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	7.6

Statistical analysis title	Vaccine Efficacy V160 2-Dose
Comparison groups	V160 2-Dose Regimen v Placebo
Number of subjects included in analysis	1089
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Vaccine Efficacy
Point estimate	-32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-135
upper limit	25

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality and serious adverse events: Up to 24 months; Non-serious adverse events: Up to 14 days following any vaccination.

Adverse event reporting additional description:

The analysis population included all randomized participants who received at least 1 injection of V160 or placebo, had safety follow-up data, and had been assigned to the treatment arm corresponding to the actual clinical material received. The all-cause mortality analysis population included all randomized participants.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	V160 3-Dose Group

Reporting group description:

Participants received V160 vaccination by intramuscular (IM) injection on Day 1, Month 2, and Month 6.

Reporting group title	V160 2-Dose Group

Reporting group description:

Participants received V160 vaccination by IM injection on Day 1 and Month 6 and placebo at Month 2.

Reporting group title	Placebo Group

Reporting group description:

Participants received placebo by IM injection on Day 1, Month 2, and Month 6.

Serious adverse events	V160 3-Dose Group	V160 2-Dose Group	Placebo Group
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 728 (3.02%)	29 / 729 (3.98%)	26 / 732 (3.55%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cervix carcinoma			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enchondromatosis			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian germ cell teratoma benign			

subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Haemorrhage			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Hypotension			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Pregnancy, puerperium and perinatal conditions			
Abortion missed			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion spontaneous			
subjects affected / exposed	2 / 728 (0.27%)	6 / 729 (0.82%)	7 / 732 (0.96%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anembryonic gestation			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	2 / 732 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eclampsia			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ectopic pregnancy			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	2 / 732 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Postpartum haemorrhage			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pre-eclampsia			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Ruptured ectopic pregnancy			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Threatened labour			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Chest pain			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Adnexal torsion			

subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Intermenstrual bleeding			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Anxiety			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	2 / 728 (0.27%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Suicidal ideation			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Suicide attempt			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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			
Ankle fracture			
subjects affected / exposed	0 / 728 (0.00%)	2 / 729 (0.27%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest injury			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Concussion			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Intentional overdose			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic bone injury			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Procedural haemorrhage			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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

Radius fracture			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Splenic rupture			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Tendon rupture			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Traumatic arthropathy			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Tachycardia			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Nervous system disorders			

Epilepsy			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Idiopathic intracranial hypertension			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain lower			
subjects affected / exposed	1 / 728 (0.14%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal ulcer			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Salivary gland calculus			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 728 (0.00%)	2 / 729 (0.27%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Renal colic			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Ureterolithiasis			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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 / 728 (0.00%)	1 / 729 (0.14%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Breast abscess			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Cellulitis			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Epstein-Barr virus infection			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (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
Infection			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Pharyngotonsillitis			
subjects affected / exposed	0 / 728 (0.00%)	1 / 729 (0.14%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 728 (0.14%)	2 / 729 (0.27%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 728 (0.00%)	0 / 729 (0.00%)	1 / 732 (0.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 728 (0.14%)	0 / 729 (0.00%)	0 / 732 (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
Urinary tract infection			

subjects affected / exposed	0 / 728 (0.00%)	2 / 729 (0.27%)	0 / 732 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	V160 3-Dose Group	V160 2-Dose Group	Placebo Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	697 / 728 (95.74%)	700 / 729 (96.02%)	557 / 732 (76.09%)
Nervous system disorders			
Headache			
subjects affected / exposed	434 / 728 (59.62%)	450 / 729 (61.73%)	368 / 732 (50.27%)
occurrences (all)	988	976	795
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	457 / 728 (62.77%)	461 / 729 (63.24%)	357 / 732 (48.77%)
occurrences (all)	1128	1077	843
Injection site erythema			
subjects affected / exposed	254 / 728 (34.89%)	208 / 729 (28.53%)	30 / 732 (4.10%)
occurrences (all)	400	273	39
Injection site pain			
subjects affected / exposed	680 / 728 (93.41%)	664 / 729 (91.08%)	239 / 732 (32.65%)
occurrences (all)	1943	1524	374
Injection site pruritus			
subjects affected / exposed	44 / 728 (6.04%)	26 / 729 (3.57%)	4 / 732 (0.55%)
occurrences (all)	54	34	5
Injection site swelling			
subjects affected / exposed	248 / 728 (34.07%)	233 / 729 (31.96%)	21 / 732 (2.87%)
occurrences (all)	404	311	26
Pyrexia			
subjects affected / exposed	75 / 728 (10.30%)	90 / 729 (12.35%)	27 / 732 (3.69%)
occurrences (all)	93	112	42
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	45 / 728 (6.18%)	55 / 729 (7.54%)	46 / 732 (6.28%)
occurrences (all)	50	68	54

Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	62 / 728 (8.52%)	65 / 729 (8.92%)	69 / 732 (9.43%)
occurrences (all)	81	80	80
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	162 / 728 (22.25%)	162 / 729 (22.22%)	76 / 732 (10.38%)
occurrences (all)	226	249	121
Myalgia			
subjects affected / exposed	455 / 728 (62.50%)	424 / 729 (58.16%)	200 / 732 (27.32%)
occurrences (all)	996	818	336
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	53 / 728 (7.28%)	53 / 729 (7.27%)	37 / 732 (5.05%)
occurrences (all)	59	56	40

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2018	Updated protocol procedures for clarification.
11 June 2019	Updated congenital cytomegalovirus infection (cCMVi) case definition, clarified the infant sample collection strategy, and adjusted visit schedules to be more accommodating and maintain more contact with study participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported