



Clinical trial results:

A Phase 2, Randomized, Double-Blind, Multicenter Study to Evaluate the Safety and Immunogenicity of Three Different Potency Levels of V181 (Dengue Quadrivalent Vaccine rDENV30 [live, attenuated]) in Healthy Adults

Summary

EudraCT number	2020-004501-30
Trial protocol	DE FI
Global end of trial date	07 May 2024

Results information

Result version number	v1 (current)
This version publication date	10 May 2025
First version publication date	10 May 2025

Trial information

Trial identification

Sponsor protocol code	V181-003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05507450
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue,, Rahway, NJ, United States, P.O. Box 2000
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	05 June 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 June 2023
Global end of trial reached?	Yes
Global end of trial date	07 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to compare the dengue virus-neutralizing antibody geometric mean titers (GMTs) for each of the 4 dengue serotypes (DENV1, DENV2, DENV3, and DENV4) at Day 28 post-vaccination for participants administered the V181 Low-Potency Level vaccine versus the V181 Mid-Potency Level vaccine. This study will also evaluate the safety and tolerability of 3 different V181 potency level vaccines. The primary hypothesis of the study is that the V181 Low-Potency Level vaccine is non-inferior to the V181 Mid-Potency Level vaccine for each of the 4 dengue serotypes based on GMTs at Day 28 post-vaccination.

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	07 September 2022
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: 230
Country: Number of subjects enrolled	Canada: 173
Country: Number of subjects enrolled	Finland: 178
Country: Number of subjects enrolled	Germany: 235
Country: Number of subjects enrolled	Israel: 152
Country: Number of subjects enrolled	Taiwan: 40
Country: Number of subjects enrolled	United States: 263
Worldwide total number of subjects	1271
EEA total number of subjects	413

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)	1271
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult males or females, in generally good health, between 18 to 50 years of age, and without a history of dengue or Zika natural infection or prior receipt of any other dengue vaccine were enrolled in this study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	V181 High-Potency Level Group

Arm description:

Participants received a single 0.5 mL subcutaneous (SC) dose of V181 High-Potency vaccine.

Arm type	Experimental
Investigational medicinal product name	V181
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single 0.5 mL subcutaneous (SC) dose of V181 High-Potency vaccine.

Arm title	V181 Mid-Potency Level Group
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Arm description:

Participants received a single 0.5 mL SC dose of V181 Mid-Potency vaccine.

Arm type	Experimental
Investigational medicinal product name	V181
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single 0.5 mL SC dose of V181 Mid-Potency vaccine.

Arm title	V181 Low-Potency Level Group
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Arm description:

Participants received a single 0.5 mL SC dose of V181 Low-Potency vaccine.

Arm type	Experimental
Investigational medicinal product name	V181
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single 0.5 mL SC dose of V181 Low-Potency vaccine.

Arm title	Placebo
Arm description:	
Participants received a single SC 0.5 mL dose of placebo.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received a single 0.5 mL SC dose of placebo.

Number of subjects in period 1	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group
Started	231	463	461
Vaccinated at baseline	231	461	459
Completed	205	430	431
Not completed	26	33	30
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	4	11	7
Randomized By Mistake Without Study Treatment	-	2	1
Participant left the country	-	-	1
Lost to follow-up	22	20	20

Number of subjects in period 1	Placebo
Started	116
Vaccinated at baseline	115
Completed	106
Not completed	10
Adverse event, serious fatal	-
Consent withdrawn by subject	3
Randomized By Mistake Without Study Treatment	-
Participant left the country	-
Lost to follow-up	7

Baseline characteristics

Reporting groups

Reporting group title	V181 High-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL subcutaneous (SC) dose of V181 High-Potency vaccine.	
Reporting group title	V181 Mid-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL SC dose of V181 Mid-Potency vaccine.	
Reporting group title	V181 Low-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL SC dose of V181 Low-Potency vaccine.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single SC 0.5 mL dose of placebo.	

Reporting group values	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group
Number of subjects	231	463	461
Age categorical			
Units: Subjects			
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)	0	0	0
Adults (18-64 years)	231	463	461
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	33.8	33.1	33.3
standard deviation	± 9.5	± 9.8	± 9.3
Sex/Gender, Customized			
Units:			
Female	129	265	262
Male	102	198	198
Undifferentiated	0	0	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	2
Asian	15	32	33
Native Hawaiian or Other Pacific Islander	1	3	2
Black or African American	5	12	14
White	207	406	400
More than one race	2	10	10

Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	31	51	55
Not Hispanic or Latino	195	396	389
Unknown or Not Reported	5	16	17

Reporting group values	Placebo	Total	
Number of subjects	116	1271	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	116	1271	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	33.2		
standard deviation	± 9.1	-	
Sex/Gender, Customized			
Units:			
Female	59	715	
Male	57	555	
Undifferentiated	0	1	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	3	
Asian	6	86	
Native Hawaiian or Other Pacific Islander	0	6	
Black or African American	9	40	
White	100	1113	
More than one race	1	23	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	20	157	
Not Hispanic or Latino	94	1074	
Unknown or Not Reported	2	40	

End points

End points reporting groups

Reporting group title	V181 High-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL subcutaneous (SC) dose of V181 High-Potency vaccine.	
Reporting group title	V181 Mid-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL SC dose of V181 Mid-Potency vaccine.	
Reporting group title	V181 Low-Potency Level Group
Reporting group description:	
Participants received a single 0.5 mL SC dose of V181 Low-Potency vaccine.	
Reporting group title	Placebo
Reporting group description:	
Participants received a single SC 0.5 mL dose of placebo.	

Primary: Dengue Virus-Neutralizing Antibody Titers, as Measured by Virus Reduction Neutralization Test (VRNT)

End point title	Dengue Virus-Neutralizing Antibody Titers, as Measured by Virus Reduction Neutralization Test (VRNT) ^[1]
End point description:	
A dengue VRNT was conducted to assess neutralizing antibody Geometric Mean Titers (GMTs) for each of the 4 dengue vaccine serotypes (DENV1, DENV2, DENV3, and DENV4) in specimens collected from participants on Day 28 post-vaccination. The population analyzed was all randomized participants without protocol deviations that could have substantially impacted the results of the immunogenicity analyses. These deviations include participant was seropositive at baseline as assessed by VRNT and missing serology results.	
End point type	Primary
End point timeframe:	
Day 28 post-vaccination	

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	178	377	380	99
Units: Titer				
geometric mean (confidence interval 95%)				
DENV1 Serotype	326.31 (256.52 to 415.08)	261.10 (220.90 to 308.61)	184.85 (153.89 to 222.03)	10.33 (8.79 to 12.14)
DENV2 Serotype	815.79 (674.69 to 986.40)	766.98 (683.66 to 860.45)	854.59 (755.07 to 967.22)	7.50 (7.50 to 7.50)
DENV3 Serotype	203.04 (162.87 to 253.12)	135.19 (115.70 to 157.97)	94.69 (78.92 to 113.61)	7.20 (6.11 to 8.48)

DENV4 Serotype	102.13 (77.08 to 135.33)	68.33 (55.80 to 83.67)	64.43 (52.42 to 79.19)	6.50 (6.50 to 6.50)
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Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Vaccine-Related Serious Adverse Events (SAEs)

End point title	Percentage of Participants With Vaccine-Related Serious Adverse Events (SAEs) ^[2]
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End point description:

An SAE is an AE that results in death, 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 will be determined by the investigator. The population analyzed was all randomized participants who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Primary
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End point timeframe:

Up to 28 days post-vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	231	461	459	115
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Injection-Site Adverse Events (AEs)

End point title	Percentage of Participants With Solicited Injection-Site Adverse Events (AEs)
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End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited injection-site AEs include pain, erythema (redness), and swelling. The population analyzed was all randomized participants who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary
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End point timeframe:

Up to 5 days post-vaccination

End point values	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	231	461	459	115
Units: Percentage of participants				
number (not applicable)				
Injection site erythema	35.5	21.7	15.0	1.7
Injection site pain	34.2	19.7	13.5	14.8
Injection site swelling	10.0	5.4	2.4	2.6

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Systemic AEs

End point title	Percentage of Participants With Solicited Systemic AEs
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End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. Solicited systemic AEs include rash, headache, fatigue (tiredness), pyrexia (oral temperature ≥ 100.4 °F or 38.0 °C), myalgia (muscle pain), and arthralgia (joint pain). The population analyzed was all randomized participants who received at least 1 dose of study intervention according to the study intervention they received.

End point type	Secondary
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End point timeframe:

Up to 28 days post-vaccination

End point values	V181 High-Potency Level Group	V181 Mid-Potency Level Group	V181 Low-Potency Level Group	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	231	461	459	115
Units: Percentage of participants				
number (not applicable)				
Fatigue	52.8	48.6	44.0	33.9
Pyrexia	10.8	7.6	5.7	0.9
Arthralgia	21.2	12.6	13.1	7.8
Myalgia	32.0	26.5	24.0	18.3
Headache	54.5	49.9	46.2	47.0
Rash	55.8	64.0	68.6	8.7

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause Mortality: Randomization up to 12 months post-vaccination; Serious Adverse Events: Vaccination up to 12 months post-vaccination; Non-Serious Adverse Events: Vaccination up to 28 Days post-vaccination

Adverse event reporting additional description:

All-cause Mortality: randomized participants; Adverse Events: randomized participants who received at least 1 dose of study intervention according to the study intervention they received

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	V181 High Potency Level
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Reporting group description:

Participants received a single 0.5 mL SC dose of V181 High-Potency vaccine

Reporting group title	V181 Mid Potency Level
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Reporting group description:

Participants received a single 0.5 mL SC dose of V181 Mid-Potency vaccine

Reporting group title	V181 Low Potency Level
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Reporting group description:

Participants received a single 0.5 mL SC dose of V181 Low-Potency vaccine

Reporting group title	Placebo
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Reporting group description:

Participants received a single 0.5 mL SC dose of placebo

Serious adverse events	V181 High Potency Level	V181 Mid Potency Level	V181 Low Potency Level
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 231 (3.46%)	9 / 461 (1.95%)	12 / 459 (2.61%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cancer			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Neuroendocrine tumour			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (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

Cancer pain			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Biochemical pregnancy			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Abortion spontaneous			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Post-traumatic stress disorder			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Psychotic disorder			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Self-destructive behaviour			

subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Suicidal ideation			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (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
Suicide attempt			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	2 / 459 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Insomnia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Depression			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament rupture			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Fibula fracture			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Meniscus injury			

subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Buttock injury			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural bile leak			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Tendon rupture			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Hypertensive heart disease			

subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Gastrointestinal disorders			
Tooth impacted			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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			
Cholecystitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chondromalacia			

subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Spinal osteoarthritis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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
Scrotal abscess			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (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
Perineal abscess			

subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	0 / 459 (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
Osteomyelitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 461 (0.00%)	1 / 459 (0.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex encephalitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 461 (0.00%)	0 / 459 (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
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 461 (0.22%)	0 / 459 (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	Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 115 (5.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Thyroid cancer			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine tumour			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cancer pain			

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Ectopic pregnancy			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Biochemical pregnancy			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Post-traumatic stress disorder			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Self-destructive behaviour			

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Insomnia			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ligament rupture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fibula fracture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniscus injury			

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Buttock injury			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural bile leak			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radius fracture			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Hypertensive heart disease			

subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Tooth impacted			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chondromalacia			

subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal osteoarthritis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vestibular neuronitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Scrotal abscess			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Perineal abscess			

subjects affected / exposed	1 / 115 (0.87%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes simplex encephalitis			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	V181 High Potency Level	V181 Mid Potency Level	V181 Low Potency Level
Total subjects affected by non-serious adverse events			
subjects affected / exposed	199 / 231 (86.15%)	402 / 461 (87.20%)	405 / 459 (88.24%)
Nervous system disorders			
Headache			
subjects affected / exposed	126 / 231 (54.55%)	230 / 461 (49.89%)	212 / 459 (46.19%)
occurrences (all)	131	240	230
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	4 / 231 (1.73%)	12 / 461 (2.60%)	24 / 459 (5.23%)
occurrences (all)	4	13	24
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	122 / 231 (52.81%)	224 / 461 (48.59%)	202 / 459 (44.01%)
occurrences (all)	125	231	212
Injection site erythema			

subjects affected / exposed occurrences (all)	85 / 231 (36.80%) 89	107 / 461 (23.21%) 108	76 / 459 (16.56%) 76
Injection site pain subjects affected / exposed occurrences (all)	80 / 231 (34.63%) 80	91 / 461 (19.74%) 92	69 / 459 (15.03%) 69
Injection site swelling subjects affected / exposed occurrences (all)	23 / 231 (9.96%) 23	25 / 461 (5.42%) 25	12 / 459 (2.61%) 12
Pyrexia subjects affected / exposed occurrences (all)	25 / 231 (10.82%) 25	35 / 461 (7.59%) 35	26 / 459 (5.66%) 26
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	13 / 231 (5.63%) 15	9 / 461 (1.95%) 12	15 / 459 (3.27%) 15
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	12 / 231 (5.19%) 12	26 / 461 (5.64%) 26	25 / 459 (5.45%) 26
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	129 / 231 (55.84%) 131	295 / 461 (63.99%) 295	315 / 459 (68.63%) 315
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	49 / 231 (21.21%) 50	58 / 461 (12.58%) 58	60 / 459 (13.07%) 60
Myalgia subjects affected / exposed occurrences (all)	74 / 231 (32.03%) 75	122 / 461 (26.46%) 125	110 / 459 (23.97%) 112
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	12 / 231 (5.19%) 12	31 / 461 (6.72%) 31	15 / 459 (3.27%) 15

Non-serious adverse events	Placebo		
Total subjects affected by non-serious			

adverse events			
subjects affected / exposed	78 / 115 (67.83%)		
Nervous system disorders			
Headache			
subjects affected / exposed	54 / 115 (46.96%)		
occurrences (all)	56		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 115 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	39 / 115 (33.91%)		
occurrences (all)	43		
Injection site erythema			
subjects affected / exposed	2 / 115 (1.74%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	18 / 115 (15.65%)		
occurrences (all)	18		
Injection site swelling			
subjects affected / exposed	3 / 115 (2.61%)		
occurrences (all)	3		
Pyrexia			
subjects affected / exposed	1 / 115 (0.87%)		
occurrences (all)	1		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 115 (2.61%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	5 / 115 (4.35%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Rash			

subjects affected / exposed occurrences (all)	10 / 115 (8.70%) 10		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	9 / 115 (7.83%) 9		
Myalgia subjects affected / exposed occurrences (all)	21 / 115 (18.26%) 21		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	4 / 115 (3.48%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 August 2022	Amendment 1: Provide the potency levels for V181 and to extend the contraception requirements from 4 weeks after administration of study intervention to 90 days after administration of study intervention.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported