



Clinical trial results:

A Double-Blind, Placebo-Controlled, Randomised Study to Assess the Durability of Effect and Safety of Nemolizumab for 24 Weeks in Subjects with Prurigo Nodularis

Summary

EudraCT number	2021-003928-32
Trial protocol	AT DE BE FR PL
Global end of trial date	11 September 2023

Results information

Result version number	v1 (current)
This version publication date	02 October 2024
First version publication date	02 October 2024

Trial information

Trial identification

Sponsor protocol code	RD.06.SPR.203890
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05052983
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 117122

Notes:

Sponsors

Sponsor organisation name	Galderma S.A.
Sponsor organisation address	Zählerweg 10, Zug, Switzerland, 6300
Public contact	Clinical Trial Information Desk, Galderma S.A., ctacoordinator@galderma.com
Scientific contact	Clinical Trial Information Desk, Galderma S.A., ctacoordinator@galderma.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	11 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 September 2023
Global end of trial reached?	Yes
Global end of trial date	11 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to assess the long-term durability of response over a 24-week period following withdrawal of nemolizumab in subjects with prurigo nodularis (PN) who previously responded to treatment in the Long-term-Extension (LTE) study RD.06.SPR.202699 (2019-004294-13).

Protection of trial subjects:

This study was conducted in accordance with Good Clinical Practice (GCP) as required by the International Council for Harmonisation (ICH) guidelines. Compliance with these requirements also constitutes conformity with the ethical principles of the Declaration of Helsinki, as well as other applicable local ethical and legal requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 January 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	Switzerland: 4
Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	Korea, Republic of: 1
Worldwide total number of subjects	34
EEA total number of subjects	27

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	22
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 14 study sites in 7 countries from 24 January 2022 to 11 September 2023.

Pre-assignment

Screening details:

A total of 34 subjects from LTE study RD.06.SPR.202699 (2019-004294-13) were enrolled and treated 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	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Nemolizumab

Arm description:

Subjects received either 1 (30 milligram [mg]) or 2 (2*30 mg) subcutaneous (SC) injection(s) of nemolizumab every 4 weeks (Q4W) for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by interactive response technology (IRT).

Arm type	Experimental
Investigational medicinal product name	Nemolizumab
Investigational medicinal product code	CD14152
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg (1 injection) or 2*30mg (2 injections) of nemolizumab SC, Q4W.

Arm title	Placebo
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Arm description:

Subjects received either 1 (30 mg) or 2 (2*30 mg) SC injection(s) of placebo Q4W for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by IRT.

Arm type	Placebo
Investigational medicinal product name	Nemolizumab placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

30 mg (1 injection) or 2*30mg (2 injections) of placebo SC, Q4W.

Number of subjects in period 1	Nemolizumab	Placebo
Started	18	16
Completed	14	4
Not completed	4	12
Adverse event	1	-
Lack of efficacy	3	12

Baseline characteristics

Reporting groups

Reporting group title	Nemolizumab
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Reporting group description:

Subjects received either 1 (30 milligram [mg]) or 2 (2*30 mg) subcutaneous (SC) injection(s) of nemolizumab every 4 weeks (Q4W) for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by interactive response technology (IRT).

Reporting group title	Placebo
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Reporting group description:

Subjects received either 1 (30 mg) or 2 (2*30 mg) SC injection(s) of placebo Q4W for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by IRT.

Reporting group values	Nemolizumab	Placebo	Total
Number of subjects	18	16	34
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	59.9 ± 14.06	59.1 ± 13.41	-
Gender categorical Units: Subjects			
Female	14	13	27
Male	4	3	7
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	13	15	28
Unknown or Not Reported	4	1	5
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	14	15	29
More than one race	0	0	0
Unknown or Not Reported	3	1	4

End points

End points reporting groups

Reporting group title	Nemolizumab
Reporting group description: Subjects received either 1 (30 milligram [mg]) or 2 (2*30 mg) subcutaneous (SC) injection(s) of nemolizumab every 4 weeks (Q4W) for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by interactive response technology (IRT).	
Reporting group title	Placebo
Reporting group description: Subjects received either 1 (30 mg) or 2 (2*30 mg) SC injection(s) of placebo Q4W for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by IRT.	

Primary: Time From Baseline to Relapse Meeting At Least 1 of the Defined Criteria

End point title	Time From Baseline to Relapse Meeting At Least 1 of the Defined Criteria
End point description: Time from baseline to relapse, defined as meeting at least 1 of the following criteria 1. Increase in (weekly average of the) Peak Pruritus Numerical Rating Scale (PP NRS) score greater than or equal to (\geq)4 points from baseline 2. Increase in Investigator's Global Assessment (IGA) score \geq 2 points from baseline. Time to relapse was censored at the last assessment of IGA and PP NRS prior to treatment discontinuation or use of prohibited medication. Intent-to-treat (ITT) population included all randomised subjects. Here, "overall number of subjects analysed" signified subjects who were evaluable for this endpoint. Here, "99999" was used as a space filler and denotes that median and 95% CI were not evaluated due to insufficient number subject with relapse.	
End point type	Primary
End point timeframe: Baseline up to Week 24	

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: Days				
median (confidence interval 95%)	99999 (99999 to 99999)	112.50 (84.00 to 161.00)		

Statistical analyses

Statistical analysis title	Nemolizumab versus Placebo
Comparison groups	Nemolizumab v Placebo

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.125
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.034
upper limit	0.462

Secondary: Percentage of Subjects who Maintained Investigator Global Assessment (IGA) Success at Each Scheduled Visit

End point title	Percentage of Subjects who Maintained Investigator Global Assessment (IGA) Success at Each Scheduled Visit
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End point description:

IGA was a 5-point scale used by the investigator or trained designee to evaluate the global severity of PN. The Investigator reviewed the subject's skin and give a score of 0 (Clear), 1 (Almost clear), 2 (Mild), 3 (Moderate), or 4 (Severe). Treatment response/success was defined as 0 (clear) or 1 (almost clear). ITT population included all randomised subjects. Here, "n" included all subjects who were evaluated for this endpoint for the specified timepoint. Observed Cases (OC) analysis is applied here, where analysis is using all the observed data at each time point, no imputation for missing data.

End point type	Secondary
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End point timeframe:

Baseline up to Week 24

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: Percentage of Subjects				
number (not applicable)				
At week 4 (n=17,15)	88.2	86.7		
At week 8 (n=17,16)	82.4	81.3		
At week 12 (n=17,15)	88.2	53.3		
At week 16 (n=16,11)	81.3	27.3		
At week 20 (n=15,7)	86.7	57.1		
At week 24 (n=14,5)	85.7	60.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Increase in Peak Pruritus (PP) Numeric Rating Scale (NRS) Score of ≥ 4 Points From Baseline at Each Scheduled Visit

End point title	Percentage of Subjects with Increase in Peak Pruritus (PP)
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End point description:

Pruritus NRS is a scale used by the subjects to report the intensity of their pruritus (itch) during the last 24 hours. For maximum itch intensity: the scores are provided on a 11-point scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable'. Higher scores indicate worse outcome. ITT population included all randomised subjects. Here, "n" included all subjects who were evaluated for this endpoint for the specified timepoint. Observed Cases (OC) analysis is applied here, where analysis is using all the observed data at each time point, no imputation for missing data.

End point type Secondary

End point timeframe:

Baseline up to Week 24

End point values	Nemolizumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	16		
Units: Percentage of subjects				
number (not applicable)				
At week 4 (n=13,13)	0	0		
At week 8 (n= 13,14)	0	0		
At week 12 (n-=16,12)	0	16.7		
At week 16 (n=15,12)	6.7	33.3		
At week 20 (n=14,6)	0	33.3		
At week 24 (n=10,5)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline up to End of study (Week 32)

Adverse event reporting additional description:

The safety population included all randomised subjects who receive at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	25.0
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Reporting groups

Reporting group title	Nemolizumab
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Reporting group description:

Subjects received either 1(30mg) or 2(2*30 mg) SC injection(s) of nemolizumab Q4W for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by IRT.

Reporting group title	Placebo
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Reporting group description:

Subjects received either 1 (30 mg) or 2 (2*30 mg) SC injection(s) of placebo Q4W for a period of 24 weeks (with last injection at Week 20). Subjects received the same dosage (1 or 2 SC injections) as received in the lead-in LTE study RD.06.SPR.202699 (2019-004294-13), as assigned by IRT.

Serious adverse events	Nemolizumab	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral ischaemia			

subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Nemolizumab	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 18 (61.11%)	10 / 16 (62.50%)	
Vascular disorders			
Diabetic macroangiopathy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Haematoma			
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
General disorders and administration site conditions			
Administration site erythema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Administration site reaction			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	3	0	
Injection site haematoma			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Vulvovaginal dryness			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Aphonia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Cough subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Wheezing subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Psychiatric disorders Depression subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Investigations Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Peak expiratory flow rate decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Urinary lipids present subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Post procedural complication subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Cardiac disorders Atrioventricular block first degree			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Extrasystoles subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Nervous system disorders Cerebrovascular disorder subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3	1 / 16 (6.25%) 3	
Post herpetic neuralgia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Seizure subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2	0 / 16 (0.00%) 0	
Dental caries subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1	0 / 16 (0.00%) 0	
Diarrhoea subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Irritable bowel syndrome subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0	1 / 16 (6.25%) 1	
Skin and subcutaneous tissue disorders			

Eczema			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Intertrigo			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Lichen planus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Neurodermatitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Skin lesion			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Endocrine disorders			
Thyroid cyst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Exostosis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Neck pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Synovial cyst			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

Bronchitis		
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	0
COVID-19		
subjects affected / exposed	2 / 18 (11.11%)	3 / 16 (18.75%)
occurrences (all)	2	3
Cystitis		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	1
Febrile infection		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	1
Gingivitis		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	1
Herpes zoster		
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)
occurrences (all)	2	0
Nasopharyngitis		
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	1	1
Oral herpes		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	2
Otitis media		
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	0
Pustule		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	1
Respiratory tract infection		
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	1

Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Sinusitis			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Tonsillitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 18 (0.00%)	2 / 16 (12.50%)	
occurrences (all)	0	2	
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Hypertriglyceridaemia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 December 2022	Following changes were made: 1) Updated planned sample size according to current enrollment projections. 2) Updated the introduction to include new nemolizumab ongoing studies and completion of PN Phase 3 pivotal study RD.06.SRE.203065. 3) Excluded clarification on double barrier method for Germany only; this was covered in a country-specific amendment (protocol version 3.0). 4) Excluded gabapentinoids alone as a prohibited therapy, as they are examples of prohibited anti-epileptics. 5) Added that a minimum 3-week interval must have occurred between doses of study drug for subjects who re-entered the LTE study. 6) Updated conditions for an interim analysis to optional (not mandatory) as it was most likely to be inconclusive due to small sample size. 7) Modified IB version from Version R11 to Version R14.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported