Clinical trial results:
Efficacy of a novel 1l PEG plus ascorbate (Plenvu) bowel preparation vs. 2l PEG plus ascorbate (Moviprep), a randomized controlled multicenter trial (PLEMO)

Summary

EudraCT number	2018-003304-39
Trial protocol	DK
Global end of trial date	10 April 2022

Results information

Result version number	v1 (current)
This version publication date	17 December 2023
First version publication date	17 December 2023

Trial information

Trial identification

Sponsor protocol code	007

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Digestive disease center, Bispebjerg Hospital
Sponsor organisation address	Bispebjerg Bakke 23, Copenhagen NV, Denmark, 2400
Public contact	Morten Rasmussen, Morten Rasmussen, morten.rasmussen@regionh.dk
Scientific contact	Morten Rasmussen, Morten Rasmussen, morten.rasmussen@regionh.dk

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	22 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 April 2022
Global end of trial reached?	Yes
Global end of trial date	10 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the bowel cleansing efficacy of either 1L PEG with ascorbate or 2L PEG with ascorbate in a randomized controlled trial including persons participating in the Danish national bowel screening program.

Protection of trial subjects:

The Danish Data Protection Agency

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 October 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 1275
Worldwide total number of subjects	1275
EEA total number of subjects	1275

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)	681
From 65 to 84 years	594
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants in the Danish national bowel cancer screening scheduled for colonoscopy at Bispebjerg Hospital will be contacted by a study nurse for the purpose of study recruitment. All participants will be offered the possibility for a consultation with an investigator prior to consenting for participation.

Pre-assignment

Screening details:

Participants scheduled for a screening colonoscopy at Bispebjerg Hospital
Age 50-74 years
Possibility for participants to recieve electronic documents
Telephone number to participants avalible

Period 1

Period 1 title	Intervention (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind[1]
Roles blinded	Investigator, Monitor, Data analyst[2]

Arms

Are arms mutually exclusive?	Yes
Arm title	Intervention (1L PEG + Asc)

Arm description:

Participants randomized to recieve intervention (1L polyethylene glycol + ascorbate)

Arm type	Experimental
Investigational medicinal product name	Plenvu
Investigational medicinal product code	A06A D65
Other name	
Pharmaceutical forms	Powder for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Powder for Oral Solution consisting of one sachet of Dose 1 and two sachets (A & B) for Dose 2.
- Dose 1 taken in the evening before the colonoscopy (approximately 18.00)
- Dose 2 taken in the early morning of the day of the colonoscopy.

Dose 1: The contents of the sachet for Dose 1 should be dissolved in 500 ml of water. The solution should be taken over a period of 30 minutes, followed by at least 500 ml of clear fluid over the next 30 minutes.
Dose 2: The contents of the two sachets (sachets A and B) for Dose 2 should be dissolved with 500 ml of water. The solution should be taken over a period of 30 minutes, followed by at least 500 ml of clear fluid over the next 30 minutes.

In addition to the fluids taken as part of the course of treatment, any amount of supplementary clear fluid (e.g. water, clear soup, fruit juice without pulp, soft drinks, tea and/or coffee without milk) may be taken.

Arm title	Control (2L PEG + Asc)

Arm description:

Participants randomized to recieve control (2L polyethylene glycol + ascorbate)

Arm type	Active comparator

Investigational medicinal product name	Moviprep
Investigational medicinal product code	A06A D
Other name	
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Dose 1 + 2: Powder for Oral Solution consisting of one sachet of Dose A and one sachet of Dose B.
- Dose 1 taken in the evening before the colonoscopy (approximately 18.00)
- Dose 2 taken in the early morning of the day of the colonoscopy.

Dose 1 + 2: The contents of sachet A and B should be dissolved in 1 litre of water. The solution should be taken over a period of one to two hours, followed by at least 500 ml of clear fluid

In addition to the fluids taken as part of the course of treatment, any amount of supplementary clear fluid (e.g. water, clear soup, fruit juice without pulp, soft drinks, tea and/or coffee without milk) may be taken.

Notes:

[1] - The number of roles blinded appears inconsistent with a single blinded trial. It is expected that there will be one role blinded in a single blind trial.
Justification: This is single-blinded (to investigator). Double blinding was not possible

[2] - The roles blinded appear inconsistent with a simple blinded trial.

Justification: This is single-blinded (to investigator). Double blinding was not possible

Number of subjects in period 1	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)
Started	629	646
Completed	615	628
Not completed	14	18
Requested colonoscopy at other hospital	-	4
Consent withdrawn by subject	-	1
Physician decision	-	1
Non appearance	3	1
Unknown reasons	-	1
Randomization allocation unclear	1	2
Rejected colonoscopy	4	6
Protocol deviation	6	2

Baseline characteristics

Reporting groups	
Reporting group title	Intervention (1L PEG + Asc)
Reporting group description:	
Participants randomized to recieve intervention (1L polyethylene glycol + ascorbate)	
Reporting group title	Control (2L PEG + Asc)
Reporting group description:	
Participants randomized to recieve control (2L polyethylene glycol + ascorbate)	

Reporting group values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)	Total
Number of subjects	629	646	1275
Age categorical Units: Subjects			
Adults (18-64 years)	335	346	681
From 65-84 years	294	300	594
Age continuous Units: years			
median	64	64	
inter-quartile range (Q1-Q3)	56 to 70	56 to 70	-
Gender categorical Units: Subjects			
Female	322	310	632
Male	307	336	643

End points

End points reporting groups

Reporting group title	Intervention (1L PEG + Asc)
Reporting group description:	
Participants randomized to recieve intervention (1L polyethylene glycol + ascorbate)	
Reporting group title	Control (2L PEG + Asc)
Reporting group description:	
Participants randomized to recieve control (2L polyethylene glycol + ascorbate)	

Primary: To evaluate the overall bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc

End point title	To evaluate the overall bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc
End point description:	
Efficacy of the bowel cleansing efficacy in the two arms were determined using the Boston Bowel Preparation Scale. All participants undergoing colonoscopy were assessed.	
End point type	Primary
End point timeframe:	
After colonoscopy	

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	628		
Units: 4				
arithmetic mean (standard deviation)				
BBPS right colon	2.54 (± 0.77)	2.30 (± 0.90)		
BBPS transverse colon	2.60 (± 0.71)	2.36 (± 0.87)		
BBPS left colon	2.63 (± 0.63)	2.39 (± 0.80)		
BBPS total	7.76 (± 1.93)	7.06 (± 2.41)		

Statistical analyses

Statistical analysis title	Wilcoxon rank sum test
Statistical analysis description:	
Efficacy will be assessed as bowel cleansing success according to the validated Boston Bowel Preparation Scale (BBPS). Bowel preparation quality will be assessed by the colonoscopist for the following colonic segments: Right colon, transverse colon and left colon. After washing and suctioning have been performed each segment is given a score from 0-3.	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)

Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	Wilcoxon (Mann-Whitney)

Notes:

[1] - Left colon, transverse colon, right colon and total scores all showed p<0.001

Primary: To evaluate the bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc in terms of adequate bowel preparation

End point title	To evaluate the bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc in terms of adequate bowel preparation

End point description:

Efficacy of the bowel cleansing efficacy in the two arms were determined using the Boston Bowel Preparation Scale. All participants undergoing colonoscopy were assessed. Data were assessed for all participants with adequate bowel preparation defined as BBPS ≥2 in each segment.

End point type	Primary

End point timeframe:

After colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	567[2]	541[3]		
Units: 4				
arithmetic mean (standard deviation)				
BBPS rigth colon	2.71 (± 0.45)	2.59 (± 0.49)		
BBPS transverse colon	2.73 (± 0.45)	2.63 (± 0.48)		
BBPS left colon	2.71 (± 0.45)	2.60 (± 0.49)		
BBPS total	8.16 (± 1.23)	7.82 (± 1.33)		

Notes:

[2] - Number of participants with a BBPS score in any segment of at least 2

[3] - Number of participants with a BBPS score in any segment of at least 2

Statistical analyses

Statistical analysis title	Wilcoxon rank sum test

Statistical analysis description:

Wilcoxon rank sum test

Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1108
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [4]
Method	Wilcoxon (Mann-Whitney)

Notes:

[4] - Left colon, transverse colon, right colon and total scores all showed p<0.001

Primary: To evaluate the bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc

in terms of excellent bowel preparation

End point title	To evaluate the bowel cleansing efficacy of 1L PEG + Asc vs. 2L PEG + Asc in terms of excellent bowel preparation

End point description:

Efficacy of the bowel cleansing efficacy in the two arms were determined using the Boston Bowel Preparation Scale. All participants undergoing colonoscopy were assessed. Data were assessed for all participants with excellent bowel preparation in each segment (BBPS =3)

End point type	Primary

End point timeframe:

After colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	613	627		
Units: Number BBPS = 3				
Right colon	405	319		
Transverse colon	420	345		
Left colon	421	336		

Statistical analyses

Statistical analysis title	Chi square

Statistical analysis description:

Number of participants with a BBPS score in any segment of 3

Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1240
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [5]
Method	Chi-squared

Notes:

[5] - Left colon, transverse colon, right colon and overall scores all showed p<0.001

Secondary: Adenoma detection rate

End point title	Adenoma detection rate

End point description:

Data on adenomas were obtained from histopathologic reports. In case of large lesions planned for subsequent polypectomy or participants on anticoagulation/antiplatelet medication a subsequent colonoscopy was performed and data from these procedures were included as well.

End point type	Secondary

End point timeframe:

During colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	628		
Units: %				
Adenoma detection rate	50	48		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants where at least one adenoma was detected	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5
Method	Chi-squared

Secondary: Cancer detection

End point title	Cancer detection
End point description:	
Data on adenomas were obtained from histopathologic reports. In case of large lesions planned for subsequent polypectomy or participants on anticoagulation/antiplatelet medication a subsequent colonoscopy was performed and data from these procedures were included as well.	
End point type	Secondary
End point timeframe:	
During colonoscopy	

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	628		
Units: number				
Number of cancers	27	24		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants detected with colorectal cancer	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)

Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Chi-squared

Secondary: Serrated lesion detection rate

End point title	Serrated lesion detection rate

End point description:

Data on adenomas were obtained from histopathologic reports. In case of large lesions planned for subsequent polypectomy or participants on anticoagulation/antiplatelet medication a subsequent colonoscopy was performed and data from these procedures were included as well.

End point type	Secondary

End point timeframe:

During colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	628		
Units: %				
Serrated lesion detection rate (%)	16	15		

Statistical analyses

Statistical analysis title	Chi square

Statistical analysis description:

Rate of participants with at least one serrated lesion detected

Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1243
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, nausea

End point title	Tolerability of the bowel preparation, nausea

End point description:

Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy

End point type	Secondary

End point timeframe:

Prior to colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Nausea	344	288		

Statistical analyses

Statistical analysis title	Chi square

Statistical analysis description:

Number of participants reporting any nausea

Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, vomit

End point title	Tolerability of the bowel preparation, vomit

End point description:

Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy

End point type	Secondary

End point timeframe:

Prior to colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Vomit	83	54		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants reporting of any comiting	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, bloating

End point title	Tolerability of the bowel preparation, bloating
End point description:	
Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy	
End point type	Secondary
End point timeframe:	
Prior to colonoscopy	

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Bloating	382	420		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants reporting of any bloating	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, headache

End point title	Tolerability of the bowel preparation, headache

End point description:

Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy

End point type	Secondary

End point timeframe:

Prior to colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Headache	214	188		

Statistical analyses

Statistical analysis title	Chi square
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.057
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, sleep interrupted

End point title	Tolerability of the bowel preparation, sleep interrupted

End point description:

Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy

End point type	Secondary

End point timeframe:

Prior to colonoscopy

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Sleep interrupted	358	376		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants reporting any disturbance of sleep	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7
Method	Chi-squared

Secondary: Tolerability of the bowel preparation, willingness to repeat

End point title	Tolerability of the bowel preparation, willingness to repeat
End point description:	
Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy	
End point type	Secondary
End point timeframe:	
Prior to colonoscopy	

End point values	Intervention (1L PEG + Asc)	Control (2L PEG + Asc)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	599	618		
Units: Condition present, %				
Willingness to repeat	492	469		

Statistical analyses

Statistical analysis title	Chi square
Statistical analysis description:	
Number of participants reporting willingness to repeat the bowel cleansing	
Comparison groups	Intervention (1L PEG + Asc) v Control (2L PEG + Asc)
Number of subjects included in analysis	1217
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Chi-squared

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day and time of colonoscopy for participants reported events
30 day follow up for complications

Adverse event reporting additional description:

Participants were asked to answer a questionnaire when arriving at the endoscopy unit, but prior to colonoscopy. This questionnaire included information about any adverse events/side effects other than asked in the questionnaire (nausea, vomit, bloating, headache and disturbance of sleep). A file look-up was made to evaluate 30 day complications.

Assessment type	Systematic

Dictionary used

Dictionary name	None
Dictionary version	unknown

Reporting groups

Reporting group title	1L PEG + Asc
Reporting group description: -	
Reporting group title	2L PEG + Asc

Reporting group description: -

Serious adverse events	1L PEG + Asc	2L PEG + Asc	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 615 (0.00%)	0 / 628 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0.1 %

Non-serious adverse events	1L PEG + Asc	2L PEG + Asc	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	75 / 615 (12.20%)	56 / 628 (8.92%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 615 (1.14%)	4 / 628 (0.64%)	
occurrences (all)	7	4	
Fatigue			
subjects affected / exposed	5 / 615 (0.81%)	3 / 628 (0.48%)	
occurrences (all)	5	3	
Headache			

subjects affected / exposed	0 / 615 (0.00%)	2 / 628 (0.32%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
Freezing			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Non function			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Unrest			
subjects affected / exposed	2 / 615 (0.33%)	3 / 628 (0.48%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 615 (0.33%)	18 / 628 (2.87%)	
occurrences (all)	2	18	
Bloating			
subjects affected / exposed	4 / 615 (0.65%)	6 / 628 (0.96%)	
occurrences (all)	4	6	
Constipation			
subjects affected / exposed	0 / 615 (0.00%)	1 / 628 (0.16%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	2 / 615 (0.33%)	0 / 628 (0.00%)	
occurrences (all)	2	0	
Dry mouth			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Fecal incontinence			
subjects affected / exposed	2 / 615 (0.33%)	1 / 628 (0.16%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	3 / 615 (0.49%)	1 / 628 (0.16%)	
occurrences (all)	3	1	
Vomiting			

subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Flu			
subjects affected / exposed	3 / 615 (0.49%)	0 / 628 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Anal discomfort			
subjects affected / exposed	14 / 615 (2.28%)	5 / 628 (0.80%)	
occurrences (all)	14	5	
Rash			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 615 (0.16%)	0 / 628 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Fever			
subjects affected / exposed	1 / 615 (0.16%)	1 / 628 (0.16%)	
occurrences (all)	1	1	
Freezing			
subjects affected / exposed	11 / 615 (1.79%)	9 / 628 (1.43%)	
occurrences (all)	11	9	
Metabolism and nutrition disorders			
Poor palatability			
subjects affected / exposed	2 / 615 (0.33%)	2 / 628 (0.32%)	
occurrences (all)	2	2	
Thirst			
subjects affected / exposed	11 / 615 (1.79%)	0 / 628 (0.00%)	
occurrences (all)	11	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported