Clinical trial results:
Reducing antibiotic use for uncomplicated urinary tract infection in general practice by treatment with Uva ursi - a comparative effectiveness trial

Summary

EudraCT number	2016-000477-21
Trial protocol	DE
Global end of trial date	20 June 2019

Results information

Result version number	v1 (current)
This version publication date	26 November 2020
First version publication date	26 November 2020

Trial information

Trial identification

Sponsor protocol code	01579

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03151603
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsmedizin der Georg-August-Universität Göttingen
Sponsor organisation address	Robert-Koch-Straße 40, Göttingen, Germany, 37075
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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	20 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 June 2019
Global end of trial reached?	Yes
Global end of trial date	20 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether antibiotic use can be reduced in women with uncomplicated UTI by treatment with Arctostaphylos uva-ursi (UU, Arctuvan), and conditional antibiotics only in case of persistent or recurrent symptoms, without significant increase in symptoms, recurrent UTI or complications.
We compare two therapeutic strategies with respect to the following hypothesis:
A Initial treatment with UU/ conditional antibiotic reduces the number of antibiotic courses within 28 days and
B Initial treatment with UU/ conditional antibiotic is non-inferior with respect to a 7-day symptom burden as compared to immediate antibiotic use.

Protection of trial subjects:

According to medicinal knowledge, disturbances because of an urinary infect vanish after three to seven days. Therefore, no additional medication is required. If disturbances persist, the responsible investigator may start an antibiotic therapy. After a patient leaves the study, further treatment is done on the general practitioner's discretion.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2017
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	Germany: 398
Worldwide total number of subjects	398
EEA total number of subjects	398

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)	349
From 65 to 84 years	49
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Women (18-75 years) with suspected UTI and with at least two Symptoms of UTI (dysuria, urgency of micturition,
frequency, lower abdominal pain) who gave theri written informed consent to participate in the study.

Pre-assignment

Screening details:

430 patients were initially planned to contribute in the trial. 398 patients were randomized, 353 patients were analyzed as per protocol.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arctuvan

Arm description:

Uva Ursi 105 mg (Arctuvan®) 3x2 tablets orally from day 0 for 5 days

placebo granules to Monuril®: 1x1 orally

Arm type	Experimental
Investigational medicinal product name	Arctuvan
Investigational medicinal product code	
Other name	Uva Ursi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

105 mg (Arctuvan®), 3x2 tablets per day orally from day 0 for 5 days

Arm title	Monuril

Arm description:

fosfomycin (Monuril®) 3 g granules orally 1x1, placebo tablets to Arctuvan 3x2 from day 0 for 5 days

Arm type	Active comparator
Investigational medicinal product name	Monuril
Investigational medicinal product code	
Other name	Fosfomycin
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

fosfomycin (Monuril®) 3 g granules orally 1x1, placebo to Arctuvan tablets 3x2 from day 0 for 5 days

Number of subjects in period 1	Arctuvan	Monuril
Started	207	191
Completed	207	191

Baseline characteristics

Reporting groups	
Reporting group title	Arctuvan
Reporting group description:	
Uva Ursi 105 mg (Arctuvan®) 3x2 tablets orally from day 0 for 5 days placebo granules to Monuril®: 1x1 orally	

Reporting group title	Monuril
Reporting group description:	
fosfomycin (Monuril®) 3 g granules orally 1x1, placebo tablets to Arctuvan 3x2 from day 0 for 5 days	

Reporting group values	Arctuvan	Monuril	Total
Number of subjects	207	191	398
Age categorical Units: Subjects			
Adults (18-64 years)	192	157	349
From 65-84 years	15	34	49
Gender categorical Units: Subjects			
Female	207	191	398
Male	0	0	0

End points

End points reporting groups

Reporting group title	Arctuvan
Reporting group description: Uva Ursi 105 mg (Arctuvan®) 3x2 tablets orally from day 0 for 5 days placebo granules to Monuril®: 1x1 orally	

Reporting group title	Monuril
Reporting group description: fosfomycin (Monuril®) 3 g granules orally 1x1, placebo tablets to Arctuvan 3x2 from day 0 for 5 days	
Subject analysis set title	Intention to treat - intervention
Subject analysis set type	Intention-to-treat
Subject analysis set description: number of patients in the intervention group, investigated as per intention-to-treat	
Subject analysis set title	Intention-to-treat - control
Subject analysis set type	Intention-to-treat
Subject analysis set description: number of patients in the control group, investigated as per intention-to-treat	
Subject analysis set title	Per protocol - intervention
Subject analysis set type	Per protocol
Subject analysis set description: number of patient in the intervention group, investigated as per protocol	
Subject analysis set title	Per protocol - control
Subject analysis set type	Per protocol
Subject analysis set description: number of patients in the control group, investigated as per protocol	

Primary: antibiotic prescriptions from day 0 to day 28

End point title	antibiotic prescriptions from day 0 to day 28
End point description: With at least one report on use or non-use of antibiotics	
End point type	Primary
End point timeframe: from day 0 to day 28 (end-of-study)	

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	189		
Units: number	92	233		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Monuril v Arctuvan
Number of subjects included in analysis	385
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon (Mann-Whitney)

Primary: symptom burden from day 0 to day 7

End point title	symptom burden from day 0 to day 7

End point description:

Symptom recording: Symptom severity will be recorded in the patient questionnaire on day 0 and in the diary/ follow-up questionnaire day 0-7. The severity of each of the four main symptoms (dysuria, urgency, frequency, lower abdominal pain) is scored from 0 (none) to 4 (very strong). The maximum symptom sum score is 16.

End point type	Primary

End point timeframe:

from day 0 to day 7

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	207	191		
Units: number	120	150		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril
Number of subjects included in analysis	398
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.8885
Method	ANCOVA
Parameter estimate	Ratio of logarithm of symptom burden

Secondary: patients with temperature >38 °C

End point title	patients with temperature >38 °C

End point description:

number of patients with temperature >38°C, day 0-7, according to patients´ statement

End point type	Secondary

End point timeframe:
from day 0 to day 7

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	3	0		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.078
Method	Regression, Logistic

Secondary: patients with worsening symptoms (impairment in symptom score)

End point title	patients with worsening symptoms (impairment in symptom score)

End point description:

Impairment by UTI: The patient questionnaire and follow-up survey contain four items to assess UTI-symptom related impairment as a patient-relevant outcome. Impairment by each symptom is scored from 0 (none) to 4 (very strong).The maximum symptom sum score is 16.
Data for impairment by UTI will be collected in the diary at days 1, 3 and 7 until day 7 and documented in eCRF. In case of ongoing symptoms patients will monitored until symptom resolution.

End point type	Secondary

End point timeframe:
from day 0 to day 7

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	16	10		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.24
Method	Regression, Logistic

Secondary: patients with prolonged symptoms

End point title	patients with prolonged symptoms
End point description:	
Patients will be followed up until symptom resolution, defined as max. 1 score point on each symptom scale.	
End point type	Secondary
End point timeframe:	
from day 0 to day 28	

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	17	12		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Monuril v Arctuvan
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.4163
Method	Regression, Logistic

Secondary: patients with pyelonephritis

End point title	patients with pyelonephritis
End point description:	
number of pyelonephritis day 0-28, according to GP´s diagnosis	
End point type	Secondary
End point timeframe:	
from day 0 to day 28	

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	8	2		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.0672
Method	Regression, Logistic

Secondary: patients with at least 1 AE

End point title	patients with at least 1 AE
End point description: proportion of patients with at least 1 AE	
End point type	Secondary
End point timeframe: from day 0 to day 28	

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	137	103		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Monuril v Arctuvan

Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.011
Method	Regression, Logistic

Secondary: patients with at least 2 AE

End point title	patients with at least 2 AE
End point description: proportion of patients with at least 2 AE	
End point type	Secondary
End point timeframe: from day 0 to day 28	

End point values	Arctuvan	Monuril		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	205	189		
Units: number	44	32		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril
Number of subjects included in analysis	394
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.25
Method	Regression, Logistic

Secondary: early relapse

End point title	early relapse
End point description:	
End point type	Secondary
End point timeframe: day 0 to 14	

End point values	Arctuvan	Monuril	Intention to treat - intervention	Intention-to-treat - control
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	207	191	207	191
Units: number	14	20	14	20

End point values	Per protocol - intervention	Per protocol - control		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	176	177		
Units: number	12	18		

Statistical analyses

Statistical analysis title	overall study analysis
Comparison groups	Arctuvan v Monuril v Intention-to-treat - control v Intention to treat - intervention
Number of subjects included in analysis	796
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1449
Method	Regression, Logistic

Statistical analysis title	overall study analysis
Comparison groups	Monuril v Arctuvan v Per protocol - control v Per protocol - intervention
Number of subjects included in analysis	751
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.1971
Method	Regression, Logistic

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from day 0 to day 28	
Assessment type	Systematic
Dictionary used	
Dictionary name	ICD
Dictionary version	10
Reporting groups	
Reporting group title	Monuril
Reporting group description: -	
Reporting group title	Arctuvan
Reporting group description: -	

Serious adverse events	Monuril	Arctuvan	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 191 (0.52%)	7 / 207 (3.38%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Fracture			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 191 (0.00%)	4 / 207 (1.93%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Monuril	Arctuvan	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	102 / 191 (53.40%)	130 / 207 (62.80%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
dorsal pain			
subjects affected / exposed	4 / 191 (2.09%)	9 / 207 (4.35%)	
occurrences (all)	4	9	
Abdominal pain			
subjects affected / exposed	5 / 191 (2.62%)	7 / 207 (3.38%)	
occurrences (all)	5	8	
edema			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
menstrual cramps			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
irregular menstruation			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
pain			

subjects affected / exposed	8 / 191 (4.19%)	10 / 207 (4.83%)	
occurrences (all)	8	11	
heartburn			
subjects affected / exposed	1 / 191 (0.52%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Migraine			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Malaise			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
strain reaction			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
serothympanon			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Pharyngitis			
subjects affected / exposed	5 / 191 (2.62%)	1 / 207 (0.48%)	
occurrences (all)	5	1	
Sinusitis			
subjects affected / exposed	1 / 191 (0.52%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Rhinitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Bronchitis			

subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Asthma			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	1 / 191 (0.52%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
Pleural effusion			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
sorrow reaction			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
unspecified adverse effect of drug or medicament			
subjects affected / exposed	0 / 191 (0.00%)	3 / 207 (1.45%)	
occurrences (all)	0	3	
traumatic rupture			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
lesion			
subjects affected / exposed	1 / 191 (0.52%)	1 / 207 (0.48%)	
occurrences (all)	1	1	
incineration			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Nervous system disorders			

Headache			
subjects affected / exposed	16 / 191 (8.38%)	22 / 207 (10.63%)	
occurrences (all)	16	23	
Epilepsy			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
prickling			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
radiokulopathy			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Eye burns			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Hordeolum			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 191 (9.95%)	5 / 207 (2.42%)	
occurrences (all)	19	5	
Vomiting			
subjects affected / exposed	4 / 191 (2.09%)	5 / 207 (2.42%)	
occurrences (all)	4	5	
Flatulence			
subjects affected / exposed	2 / 191 (1.05%)	1 / 207 (0.48%)	
occurrences (all)	2	1	
obstipation			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			

Urinary tract infection			
subjects affected / exposed	32 / 191 (16.75%)	65 / 207 (31.40%)	
occurrences (all)	32	66	
Dysuria			
subjects affected / exposed	4 / 191 (2.09%)	6 / 207 (2.90%)	
occurrences (all)	4	6	
Polyuria			
subjects affected / exposed	2 / 191 (1.05%)	2 / 207 (0.97%)	
occurrences (all)	2	2	
Pyelonephritis			
subjects affected / exposed	1 / 191 (0.52%)	2 / 207 (0.97%)	
occurrences (all)	1	2	
hematuria			
subjects affected / exposed	2 / 191 (1.05%)	0 / 207 (0.00%)	
occurrences (all)	2	0	
Gallstone			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
nephrosis			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Endocrine disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Stenosis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 191 (0.00%)	7 / 207 (3.38%)	
occurrences (all)	0	7	

Acute infection of the upper respiratory tract			
subjects affected / exposed	12 / 191 (6.28%)	8 / 207 (3.86%)	
occurrences (all)	12	8	
bladder infection			
subjects affected / exposed	0 / 191 (0.00%)	2 / 207 (0.97%)	
occurrences (all)	0	2	
vaginal yeast infection			
subjects affected / exposed	1 / 191 (0.52%)	2 / 207 (0.97%)	
occurrences (all)	1	2	
Vaginal infection			
subjects affected / exposed	2 / 191 (1.05%)	0 / 207 (0.00%)	
occurrences (all)	2	0	
Infection			
subjects affected / exposed	1 / 191 (0.52%)	3 / 207 (1.45%)	
occurrences (all)	1	3	
Laryngitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	2	0	
Herpes virus infection			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Epicondylitis			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Abscess jaw			
subjects affected / exposed	1 / 191 (0.52%)	0 / 207 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
anorexia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 191 (0.00%)	1 / 207 (0.48%)	
occurrences (all)	0	1	
Hyperglycaemia			

subjects affected / exposed occurrences (all)	0 / 191 (0.00%) 0	1 / 207 (0.48%) 1	

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? Yes

Date	Interruption	Restart date
22 December 2017	Due to a shortage of medication, there was a temporary halt of recruitment for some trial sites from December 22th 2017 to February 19th 2018.	19 February 2018

Notes:

Limitations and caveats

None reported