Clinical trial results:
KAND567 Versus Placebo in Subjects Hospitalized with COVID-19. A Phase II, Randomized, 2-Arm Parallel-Group, Double-blind Study to Evaluate Efficacy, Safety, Tolerability, and Pharmacokinetics.

Summary

EudraCT number	2020-002322-85
Trial protocol	SE DK
Global end of trial date	07 August 2021

Results information

Result version number	v1 (current)
This version publication date	02 July 2022
First version publication date	02 July 2022

Trial information

Trial identification

Sponsor protocol code	KAN0006

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Kancera AB
Sponsor organisation address	Karolinska Institutet Science Park, Nanna Svartz Väg 4, Solna, Sweden, SE-171 65
Public contact	Niclas Brynne, PhD, Kancera AB, +46 (0)8 50 12 60 80, niclas.brynne@kancera.com
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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	07 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 August 2021
Global end of trial reached?	Yes
Global end of trial date	07 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the impact of oral administration of KAND567 versus placebo, in COVID-19 subjects admitted to the hospital for care of COVID-19 infection with respect to rates of adverse events (AEs) and serious adverse events (SAEs).

Protection of trial subjects:

The external Safety Review Committee (SRC) consisted of 3 members representing appropriate clinical expertise and having extensive experience in clinical study design and conduct. No formal statistical interim analysis was to be performed, but the SRC was to evaluate all available efficacy and safety data after 10 and 20 patients had completed the 7 day treatment period. Based on this evaluation, the SRC was to give a recommendation either to continue as planned, modify the study design, or stop the study prematurely. Their recommendation was to be discussed and agreed with the Sponsor’s CMO, who was responsible for making the ultimate decision.
SRC meetings consisted of an open session, based on the fully blinded dataset, to discuss general study issues. This was followed by the closed portion of the meeting, for SRC members only, to discuss the unblinded dataset (produced by an independent external programmer).

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	11 October 2020
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	Sweden: 34
Country: Number of subjects enrolled	Denmark: 1
Worldwide total number of subjects	35
EEA total number of subjects	35

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)	32
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

COVID-19 patients admitted to the hospital received Best Supportive Care and could be screened for inclusion in the study. If all the criteria for study participation were fulfilled and informed consent was signed, the subject was enrolled and randomized to one of the two treatment arms.

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, Monitor, Carer

Blinding implementation details:

The placebo was identical in appearance to KAND567, and the site staff, sponsor and CRO were blinded throughout the study. The staff at Tamro (responsible for labeling) and the staff at Q&Q Labs AB (responsible for bioanalysis) were unblinded. The independent Safety Review Committee (SRC) was also unblinded during the closed portion of their meetings, which was supported by the external, unblinded programmer who produced the dataset.

Arms

Are arms mutually exclusive?	Yes
Arm title	KAND567 (250 mg BID)

Arm description:

KAND567 (250 mg) was orally administered every 12 hours (at 8am and 8pm ± 1 hour) with an initial loading dose of either 250 mg or 500 mg KAND567, depending on the time of inclusion (see below).
The initial loading dose of KAND567 was given as follows:
- 500 mg was given to patients when included in the study 12 to 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)
- 250 mg was given to patients when included in the study less than 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)

Arm type	Experimental
Investigational medicinal product name	KAND567
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

KAND567 (250 mg) was orally administered every 12 hours (at 8am and 8pm ± 1 hour) with an initial loading dose of either 250 mg or 500 mg KAND567, depending on the time of inclusion (see below).
The initial loading dose of KAND567 was given as follows:
- 500 mg was given to patients when included in the study 12 to 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)
- 250 mg was given to patients when included in the study less than 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)

Arm title	Placebo

Arm description:

Placebo was orally administered every 12 hours (at 8am and 8pm ± 1 hour)

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo was orally administered every 12 hours (at 8am and 8pm ± 1 hour)

Number of subjects in period 1	KAND567 (250 mg BID)	Placebo
Started	16	19
Completed	12	16
Not completed	4	3
Adverse event, serious fatal	1	-
Consent withdrawn by subject	3	3

Baseline characteristics

Reporting groups

Reporting group title	KAND567 (250 mg BID)

Reporting group description:

KAND567 (250 mg) was orally administered every 12 hours (at 8am and 8pm ± 1 hour) with an initial loading dose of either 250 mg or 500 mg KAND567, depending on the time of inclusion (see below).
The initial loading dose of KAND567 was given as follows:
- 500 mg was given to patients when included in the study 12 to 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)
- 250 mg was given to patients when included in the study less than 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)

Reporting group title	Placebo

Reporting group description:

Placebo was orally administered every 12 hours (at 8am and 8pm ± 1 hour)

Reporting group values	KAND567 (250 mg BID)	Placebo	Total
Number of subjects	16	19	35
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)	14	18	32
From 65-84 years	2	1	3
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	5	7	12
Male	11	12	23

Subject analysis sets

Subject analysis set title	KAND567 (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

Randomized subjects who received any dose of KAND567 and for whom any post-dose data were available. Subjects were to be analyzed according to the treatment they actually received.

Subject analysis set title	Placebo (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

Randomized subjects who received any dose of placebo and for whom any post-dose data were available. Subjects were to be analyzed according to the treatment they actually received.

Reporting group values	KAND567 (Safety Analysis Set)	Placebo (Safety Analysis Set)	
Number of subjects	15	18	
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)	13	18	
From 65-84 years	2	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	5	7	
Male	10	11	

End points

End points reporting groups

Reporting group title	KAND567 (250 mg BID)

Reporting group description:

KAND567 (250 mg) was orally administered every 12 hours (at 8am and 8pm ± 1 hour) with an initial loading dose of either 250 mg or 500 mg KAND567, depending on the time of inclusion (see below).
The initial loading dose of KAND567 was given as follows:
- 500 mg was given to patients when included in the study 12 to 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)
- 250 mg was given to patients when included in the study less than 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)

Reporting group title	Placebo

Reporting group description:

Placebo was orally administered every 12 hours (at 8am and 8pm ± 1 hour)

Subject analysis set title	KAND567 (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

Randomized subjects who received any dose of KAND567 and for whom any post-dose data were available. Subjects were to be analyzed according to the treatment they actually received.

Subject analysis set title	Placebo (Safety Analysis Set)
Subject analysis set type	Safety analysis

Subject analysis set description:

Randomized subjects who received any dose of placebo and for whom any post-dose data were available. Subjects were to be analyzed according to the treatment they actually received.

Primary: Number of Adverse Events

End point title	Number of Adverse Events[1]

End point description:

End point type	Primary

End point timeframe:

The AE reporting period started at the first administration of IMP and ended at the last FU visit.

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: No statistical analyses were performed for this endpoint.

End point values	KAND567 (Safety Analysis Set)	Placebo (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	18		
Units: occurrences	71	70		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Serious Adverse Events

End point title	Number of Serious Adverse Events[2]

End point description:

End point type	Primary

End point timeframe:

The AE reporting period started at the first administration of IMP and ended at the last follow-up visit.

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: No statistical analyses were performed for this endpoint.

End point values	KAND567 (Safety Analysis Set)	Placebo (Safety Analysis Set)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	18		
Units: occurrences	5	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The AE reporting period started at the first administration of IMP and ended at the last follow-up visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	KAND567

Reporting group description:

KAND567 (250 mg) was orally administered every 12 hours (at 8am and 8pm ± 1 hour) with an initial loading dose of either 250 mg or 500 mg KAND567, depending on the time of inclusion (see below).
The initial loading dose of KAND567 was given as follows:
- 500 mg was given to patients when included in the study 12 to 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)
- 250 mg was given to patients when included in the study less than 6 hours prior to a scheduled dose (at 8 am or 8 pm ± 1 hour)

Reporting group title	Placebo

Reporting group description:

Placebo was orally administered every 12 hours (at 8am and 8pm ± 1 hour)

Serious adverse events	KAND567	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 15 (33.33%)	2 / 18 (11.11%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	1	0	
Investigations			
Myocardial strain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	3 / 15 (20.00%)	0 / 18 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypoxia			

subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	KAND567	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	17 / 18 (94.44%)	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Chills			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Pyrexia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Laryngeal pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Confusional state			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Mental fatigue			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Panic attack			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Investigations			
Fibrin D dimer increased			
subjects affected / exposed	4 / 15 (26.67%)	5 / 18 (27.78%)	
occurrences (all)	4	5	
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	4 / 15 (26.67%)	3 / 18 (16.67%)	
occurrences (all)	4	3	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	3 / 18 (16.67%)	
occurrences (all)	1	3	
Aspartate aminotransferase increased			

subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)		
occurrences (all)	1	1		
Blood alkaline phosphate increased				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
Blood creatine phosphokinase MB increased				
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
Blood creatine phosphokinase increased				
subjects affected / exposed	2 / 15 (13.33%)	0 / 18 (0.00%)		
occurrences (all)	2	0		
Blood glucose increased				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
Blood lactate dehydrogenase abnormal				
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
Blood lactate dehydrogenase increased				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
Blood pressure diastolic increased				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
Blood urea increased				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
C-reactive protein increased				
subjects affected / exposed	3 / 15 (20.00%)	1 / 18 (5.56%)		
occurrences (all)	3	1		
Electrocardiogram T wave inversion				
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
Gamma-glutamyltransferase increased				

subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Hepatic enzyme increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Liver function test increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Neutrophil count increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
PO2 decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Pulmonary arterial pressure increased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
Serum ferritin increased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
Transaminases increased			
subjects affected / exposed	2 / 15 (13.33%)	3 / 18 (16.67%)	
occurrences (all)	2	3	
Troponin increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
White blood cell count increased			
subjects affected / exposed	2 / 15 (13.33%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			

Concussion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 15 (0.00%)	2 / 18 (11.11%)	
occurrences (all)	0	2	
Paraesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Thrombocytosis			
subjects affected / exposed	2 / 15 (13.33%)	4 / 18 (22.22%)	
occurrences (all)	2	4	
Anaemia			
subjects affected / exposed	2 / 15 (13.33%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Leukocytosis			
subjects affected / exposed	2 / 15 (13.33%)	2 / 18 (11.11%)	
occurrences (all)	2	2	
Neutrophilia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	

Frequent bowel movements			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Gastroesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Glossodynia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 15 (20.00%)	2 / 18 (11.11%)	
occurrences (all)	3	2	
Stomatitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Alopecia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 18 (11.11%)	
occurrences (all)	1	2	
Rash			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	3 / 15 (20.00%)	4 / 18 (22.22%)	
occurrences (all)	3	4	
Glycosuria			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Haematuria			

subjects affected / exposed	2 / 15 (13.33%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Muscle twitching			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Erythema migrans			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 18 (5.56%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 December 2020	Sweden: Changes to inclusion/exclusion criteria, clarifications made regarding restricted medications, secondary endpoints, sampling, and treatment discontinuation, and dosing diary implemented.
04 March 2021	Denmark: Change to inclusion/exclusion criteria and the sponsor’s medical representative, clarifications made regarding timing of assessments, and dosing diary implemented.
31 May 2021	Sweden: Changes to inclusion/exclusion criteria and sponsor's medical representative, and clarifications made regarding timing of assessments.
29 June 2021	Sweden: Change in the primary objective and endpoint.
19 July 2021	Denmark: Change in the primary objective and endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported