Clinical trial results:
A 12-week randomized, participant-and investigator-blinded, placebo-controlled, parallel group study to explore the efficacy, pharmacodynamics, safety, and pharmacokinetics of two doses of inhaled CSJ117 in adults with Chronic Obstructive Pulmonary Disease (COPD)

Summary

EudraCT number	2021-000692-36
Trial protocol	FR HU DE BE CZ
Global end of trial date	15 September 2022

Results information

Result version number	v1 (current)
This version publication date	30 September 2023
First version publication date	30 September 2023

Trial information

Trial identification

Sponsor protocol code	CCSJ117B12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04882124
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, novartis.email@novartis.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	15 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 September 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the trial was to assess the effect of CSJ117 on disease/symptom burden after 12 Weeks of treatment.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2021
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	Australia: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Czechia: 8
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Japan: 3
Country: Number of subjects enrolled	United States: 15
Worldwide total number of subjects	37
EEA total number of subjects	17

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)	10
From 65 to 84 years	26
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study was conducted across 15 centers in 6 countries.

Pre-assignment

Screening details:

Eligible participants underwent screening assessments for up to 2 Weeks prior to entering the 2-Week run-in period. During the run-in period, participants had baseline assessments prior to being randomized into the treatment period. Eligible participants were stratified by eosinophil levels and randomized 1:1:1 to the 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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	CSJ117 8mg

Arm description:

Intervention: Drug: CSJ117

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

CSJ117 8 mg oral inhaled once daily over 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 4mg

Arm description:

Intervention: Drug: CSJ117

Arm type	Experimental
Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

CSJ117 4 mg oral inhaled once daily over 12 weeks. Delivered via Concept1 device.

Arm title	CSJ117 Placebo

Arm description:

Intervention: Drug: Placebo

Arm type	Placebo

Investigational medicinal product name	CSJ117
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder, hard capsule
Routes of administration	Inhalation use

Dosage and administration details:

Placebo oral inhaled once daily over 12 weeks. Delivered via Concept1 device.

Number of subjects in period 1	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo
Started	11	16	10
Completed	3	3	4
Not completed	8	13	6
Consent withdrawn by subject	-	2	-
Study terminated by sponsor	8	11	5
Protocol deviation	-	-	1

Baseline characteristics

Reporting groups	
Reporting group title	CSJ117 8mg
Reporting group description:	
Intervention: Drug: CSJ117	
Reporting group title	CSJ117 4mg
Reporting group description:	
Intervention: Drug: CSJ117	
Reporting group title	CSJ117 Placebo
Reporting group description:	
Intervention: Drug: Placebo	

Reporting group values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo
Number of subjects	11	16	10
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)	3	5	2
From 65-84 years	8	11	7
85 years and over	0	0	1
Age Continuous Units: years			
arithmetic mean	67.0	67.9	68.4
standard deviation	± 7.35	± 7.55	± 8.45
Sex: Female, Male Units: Participants			
Female	6	11	2
Male	5	5	8
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	2
White	9	14	7
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Total		
Number of subjects	37		

Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	10		
From 65-84 years	26		
85 years and over	1		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Participants			
Female	19		
Male	18		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	3		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	4		
White	30		
More than one race	0		
Unknown or Not Reported	0		

End points

End points reporting groups

Reporting group title	CSJ117 8mg
Reporting group description: Intervention: Drug: CSJ117	
Reporting group title	CSJ117 4mg
Reporting group description: Intervention: Drug: CSJ117	
Reporting group title	CSJ117 Placebo
Reporting group description: Intervention: Drug: Placebo	

Primary: Change from baseline to week 12 in E-RS score

End point title	Change from baseline to week 12 in E-RS score[1]

End point description:

The Evaluating Respiratory Symptoms (E-RS) scale is based on the 11 respiratory symptom items included in the Exacerbations of Chronic Pulmonary Disease (EXACT) Tool (a validated 14-item electronic questionnaire). These 11 items generate a total score of 0-40, with higher scores indicating more severe respiratory symptoms.

End point type	Primary

End point timeframe:

Baseline, week 12

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 analysis was performed.

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	4	
Units: score on a scale				
arithmetic mean (standard deviation)	-2.7 (± 1.72)	-1.1 (± 8.91)	-0.1 (± 3.46)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in CAT score

End point title	Change from baseline to week 12 in CAT score

End point description:

The COPD assessment test (CAT) is a short instrument used to quantify the symptom burden of COPD and will be used to assess the health status of participants. The assessment consists of 8 items, each presented as a semantic 6-point differential scale, providing a total score of 0-40. A higher score indicates a worse health status.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	4	
Units: score on a scale				
arithmetic mean (standard deviation)	-1.3 (± 9.07)	-8.0 (± 14.80)	-2.8 (± 5.38)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to week 12 in SGRQ-C score

End point title	Change from baseline to week 12 in SGRQ-C score

End point description:

The St. George Respiratory Questionnaire for COPD patients Specific Version (SGRQ-C) contains 40 items divided into two parts covering three aspects of health related to COPD: symptoms, activity and impacts. Total score ranges between 0 and 100, with higher scores indicating greater impairment of health status.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	4	
Units: Score on a scale				
arithmetic mean (standard deviation)	-2.7 (± 3.57)	-31.1 (± 49.37)	-6.1 (± 18.85)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with response in E-RS total score decrease from baseline to week 12

End point title	Number of participants with response in E-RS total score decrease from baseline to week 12

End point description:

The Evaluating Respiratory Symptoms (E-RS) scale is based on the 11 respiratory symptom items included in the Exacerbations of Chronic Pulmonary Disease (EXACT) Tool (a validated 14-item

electronic questionnaire). These 11 items generate a total score of 0-40, with higher scores indicating more severe respiratory symptoms. Response in E-RS total score is defined as a decrease of at least 1.5 points from baseline to week 12.

End point type	Secondary

End point timeframe:

Baseline, week 12

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	4	
Units: participants	2	1	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Response in CAT in total score decrease from baseline to week 12

End point title	Response in CAT in total score decrease from baseline to week 12

End point description:

The COPD assessment test (CAT) is a short instrument used to quantify the symptom burden of COPD and will be used to assess the health status of participants. The assessment consists of 8 items, each presented as a semantic 6-point differential scale, providing a total score of 0-40. A higher score indicates a worse health status. Response in CAT total score is defined as a decrease of at least 1.5 points from baseline to week 12.

End point type	Secondary

End point timeframe:

Baseline, week 12

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	3	4	
Units: Participants	1	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Response in SGRQ-C in total score decrease from baseline to week 12

End point title	Response in SGRQ-C in total score decrease from baseline to week 12

End point description:

The St. George Respiratory Questionnaire for COPD patients Specific Version (SGRQ-C) contains 40 items divided into two parts covering three aspects of health related to COPD: symptoms, activity and impacts. Total score ranges between 0 and 100, with higher scores indicating greater impairment of health status. Response in SGRQ-C total score is defined as a decrease of at least 1.5 points from baseline to week 12.

End point type	Secondary

End point timeframe:

Baseline, week 12

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	2	4	
Units: Participants	1	1	3	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in trough FEV1 after 2, 6, and 12 weeks of treatment

End point title	Change from baseline in trough FEV1 after 2, 6, and 12 weeks of treatment

End point description:

Forced expiratory volume in 1 second (FEV1) is the amount of air which can be forcibly exhaled from the lungs in the first second of a forced exhalation, measured through spirometry testing. The Number of Subjects Analyzed differs as stated on the first column for each row.

End point type	Secondary

End point timeframe:

Baseline, 2, 6 and 12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	13	10	
Units: Liter				
arithmetic mean (standard deviation)				
Week 2 – 15 minutes Pre Dose (n=11,13,10)	0.0232 (± 0.07951)	-0.0459 (± 0.16803)	0.0443 (± 0.22652)	
Week 6 – 15 minutes Pre Dose (n=9,8,6)	0.0231 (± 0.11984)	-0.0724 (± 0.14150)	-0.0582 (± 0.06159)	
Week 12 – 15 minutes Pre Dose (n=3,3,4)	0.0583 (± 0.09464)	-0.0617 (± 0.20057)	-0.0170 (± 0.05063)	

Statistical analyses

No statistical analyses for this end point

Secondary: Puffs of rescue medication per day

End point title	Puffs of rescue medication per day

End point description:

Puffs of rescue med per day as captured by electronic diary

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3	4	4	
Units: number of puffs per day				
arithmetic mean (standard deviation)	3.3370 (± 2.50242)	3.7727 (± 3.90345)	2.0987 (± 2.37543)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to COPD exacerbations via EXACT

End point title	Time to COPD exacerbations via EXACT

End point description:

Time to COPD exacerbations based on the Exacerbations of Chronic Pulmonary Disease (EXACT) tool. Symptom-defined COPD exacerbations identified by the EXACT instrument (EXACT-defined exacerbations) are defined as a persistent increase from baseline in total EXACT score of ≥ 9 points for 3 consecutive days or ≥ 12 points for 2 consecutive days. The analysis could not be performed due to the limited number of participants and observations and was removed from the Statistical Analysis Plan (SAP).

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: days				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[2] - The analysis could not be performed due to the limited number of participants.

[3] - The analysis could not be performed due to the limited number of participants.

[4] - The analysis could not be performed due to the limited number of participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and severity of COPD exacerbations via EXACT

End point title	Rate and severity of COPD exacerbations via EXACT

End point description:

Rate and severity of COPD exacerbations based on the Exacerbations of chronic obstructive pulmonary disease tool (EXACT). Symptom-defined COPD exacerbations identified by the EXACT instrument (EXACT-defined exacerbations) are defined as a persistent increase from baseline in total EXACT score of ≥ 9 points for 3 consecutive days or ≥ 12 points for 2 consecutive days. The analysis could not be performed due to the limited number of participants and observations and was removed from the Statistical Analysis Plan (SAP).

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[5]	0[6]	0[7]	
Units: Number of exacerbations				

Notes:

[5] - The analysis could not be performed due to the limited number of participants.

[6] - The analysis could not be performed due to the limited number of participants.

[7] - The analysis could not be performed due to the limited number of participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to COPD exacerbations via healthcare resource utilization (HCRU) defined exacerbations

End point title	Time to COPD exacerbations via healthcare resource utilization (HCRU) defined exacerbations

End point description:

Time to COPD exacerbations for healthcare resource utilization (HCRU) defined exacerbations. A healthcare resource utilization (HCRU)-defined exacerbation is defined as an acute worsening of respiratory symptoms (consisting of at least 2 of the following symptoms: dyspnea, cough, sputum volume, sputum purulence, chest tightness or wheeze) that requires a change in treatment.
The analysis could not be performed due to the limited number of participants and observations.

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[8]	0[9]	0[10]	
Units: days				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[8] - The analysis could not be performed due to the limited number of participants.

[9] - The analysis could not be performed due to the limited number of participants.

[10] - The analysis could not be performed due to the limited number of participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate and severity of COPD exacerbations for healthcare resource utilization (HCRU) defined exacerbations

End point title	Rate and severity of COPD exacerbations for healthcare resource utilization (HCRU) defined exacerbations

End point description:

Rate and severity of COPD exacerbations based on the Health Care Resource Utilization (HCRU). A healthcare resource utilization (HCRU)-defined exacerbation is defined as an acute worsening of respiratory symptoms (consisting of at least 2 of the following symptoms: dyspnea, cough, sputum volume, sputum purulence, chest tightness or wheeze) that requires a change in treatment.

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	16	10	
Units: Number of exacerbations				
Moderate exacerbations	2	7	2	
Severe exacerbations	0	1	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose trough concentration (Ctrough) of CSJ117

End point title	Pre-dose trough concentration (Ctrough) of CSJ117[11]

End point description:

To assess pharmacokinetic (PK) parameters of CSJ117 based on total serum concentrations.
The Number of Subjects Analyzed differs as stated on the first column for each row.

End point type	Secondary

End point timeframe:

pre-dose on Day 1, Week 2, 6 and 12

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK was not analyzed for participants receiving Placebo.

End point values	CSJ117 8mg	CSJ117 4mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	16		
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 (n=11, 16)	0 (± 0)	0 (± 0)		
Week 2 (n=11, 15)	10.5 (± 4.80)	6.03 (± 6.96)		
Week 6 (n=9, 8)	21.8 (± 15.2)	9.42 (± 6.54)		
Week 12 (n=3, 3)	51.4 (± 45.1)	38.9 (± 41.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation ratio (Racc) of CSJ117

End point title	Accumulation ratio (Racc) of CSJ117

End point description:

To assess PK parameters of CSJ117 based on total serum concentrations.
The analysis could not be performed due to the limited number of participants and observations.

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	0[12]	0[13]	0[14]	
Units: ratio				
arithmetic mean (standard deviation)	()	()	()	

Notes:

[12] - The analysis could not be performed due to the limited number of participants.

[13] - The analysis could not be performed due to the limited number of participants.

[14] - The analysis could not be performed due to the limited number of participants.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with anti-drug antibodies

End point title	Number of participants with anti-drug antibodies

End point description:

Number of participants with anti-drug antibodies at any visit

End point type	Secondary

End point timeframe:

12 weeks

End point values	CSJ117 8mg	CSJ117 4mg	CSJ117 Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	11	16	10	
Units: participants	10	11	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus 55 days post treatment, up to a maximum duration of 20 weeks.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	CSJ117 8mg

Reporting group description:

CSJ117 8mg

Reporting group title	Placebo

Reporting group description:

Placebo

Reporting group title	CSJ117 4mg

Reporting group description:

CSJ117 4mg

Serious adverse events	CSJ117 8mg	Placebo	CSJ117 4mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	CSJ117 8mg	Placebo	CSJ117 4mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 11 (36.36%)	5 / 10 (50.00%)	9 / 16 (56.25%)
Investigations			
Urinary occult blood positive			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Carpal tunnel syndrome			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 11 (18.18%)	1 / 10 (10.00%)	4 / 16 (25.00%)
occurrences (all)	2	0	7
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Gastroenteritis viral			
subjects affected / exposed	1 / 11 (9.09%)	0 / 10 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin infection			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 11 (0.00%)	1 / 10 (10.00%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 11 (0.00%)	0 / 10 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2021	The protocol was amended to allow for a shortened run-in period, and clarify ambiguity in the protocol by eliminating linguistic errors and inconsistencies. Recruitment for the study has not been initiated as of the time of this protocol amendment finalization.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported