Clinical trial results:
A Three-Arm, Randomized, Placebo-Controlled, Double-Blind Phase 3 Study to Evaluate the Safety and Efficacy of Once-Daily and Twice-Daily Dosing of a Novel Hydrocortisone Acetate 90 mg Suppository Formulation Administered with the Sephure® Suppository Applicator in Subjects with
Ulcerative Colitis of the Rectum.

Summary

EudraCT number	2019-003596-19
Trial protocol	DE IT RO DK BG
Global end of trial date	19 September 2024

Results information

Result version number	v1 (current)
This version publication date	16 March 2026
First version publication date	16 March 2026
Summary attachment (see zip file)	CHS1221 Summary (CHS1221 CSR Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	CHS1221

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04469686
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cristcot HCA LLC
Sponsor organisation address	9 Damonmill Square, Suite 4A, Concord, United States, 01742
Public contact	Jennifer J. Davagian, Cristcot HCA LLC, 978 2126380, jennifer.davagian@cristcot.com
Scientific contact	Mark C. Ensign, Cristcot HCA LLC, 978 2126380, mark.ensign@cristcot.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	19 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 September 2024
Global end of trial reached?	Yes
Global end of trial date	19 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of two dosage regimens of the study drug (hydrocortisone acetate 90 mg suppository) administered with the Sephure suppository applicator compared to placebo in the treatment of ulcerative colitis (UC) of the rectum using the Modified Mayo Score.

Protection of trial subjects:

This study was conducted as specified in Protocol CHS1221 and in compliance with the International Council for Harmonization Good Clinical Practice (GCP) and other applicable regulatory requirements. Informed consent was obtained from a subject before enrollment into the study according to regulatory and legal requirements of the participating country. The consent form was dated and retained by the Investigator as part of the study records. The Investigator was not to perform any investigation specifically required only for the clinical study until valid consent was obtained. The date of consent was documented in the Electronic Data Capture (EDC) system. Subjects were to be given ample opportunity to inquire about the details of the study, and to make the willful decision whether or not to participate in the study.

Subjects were withdrawn from the investigational product if any of the following criteria were met:
• Subject experienced an AE that was considered related to the study treatment or study procedure and was severe enough in nature to warrant treatment discontinuation. The Investigator, in conjunction with the Global Medical Monitor, could decide to withdraw the subject for safety reasons.
• Treatment with a prohibited medication was needed.
• An increase in medication for the treatment of UC was needed.
• Subject reached any safety stopping criteria (outlined in CSR).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 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	Poland: 83
Country: Number of subjects enrolled	Romania: 106
Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Bulgaria: 8
Country: Number of subjects enrolled	Denmark: 14
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Georgia: 7

Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	India: 79
Country: Number of subjects enrolled	Jordan: 24
Country: Number of subjects enrolled	Lebanon: 11
Country: Number of subjects enrolled	Moldova, Republic of: 29
Country: Number of subjects enrolled	Philippines: 69
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	South Africa: 14
Country: Number of subjects enrolled	Ukraine: 5
Country: Number of subjects enrolled	United States: 236
Country: Number of subjects enrolled	Türkiye: 20
Country: Number of subjects enrolled	Saudi Arabia: 3
Country: Number of subjects enrolled	Viet Nam: 2
Worldwide total number of subjects	784
EEA total number of subjects	266

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)	710
From 65 to 84 years	74
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Date of First Consent: 24 Sep 2020
Date of Last Patient Last Visit: 19 Sep 2024
Subject Recruitment: 784 screened; 200 randomized
Territories: Denmark, France, South Africa, Saudi Arabia, Bulgaria, Georgia, Jordan, Lebanon, Romania, Turkey, Moldova, Ukraine, Russia, Vietnam, India, Poland, Germany, Italy, Spain, Philippines, USA

Pre-assignment

Screening details:

For trial participation, subjects were required to meet all inclusion criteria (such as 18+ years of age, confirmed diagnosis and symptoms meeting criteria, able to sign informed consent, etc.) and were excluded if they met any of the exclusion criteria for the study (such as taking certain medications, certain medical histories, etc.).

Pre-assignment period milestones

Number of subjects started	784
Number of subjects completed	200

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Physician decision: 584

Period 1

Period 1 title	Dosing (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Arm A participants were given hydrocortisone acetate 90 mg suppositories twice a day.

Arm type	Experimental
Investigational medicinal product name	hydrocortisone acetate suppository
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

Hydrocortisone acetate 90 mg rectal suppository administered twice daily, morning and evening, with the Sephure suppository applicator.

Arm title	Arm B

Arm description:

Arm B participants were only given hydrocortisone acetate 90 mg suppositories once a day.

Arm type	Experimental

Investigational medicinal product name	hydrocortisone acetate suppository
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

Hydrocortisone acetate 90 mg rectal suppository administered once daily, in the morning, with the Sephure suppository applicator and a placebo dose, given in a double-dummy manner, in the evening.

Arm title	Arm C

Arm description:

Arm C participants were only given a placebo suppository.

Arm type	Placebo
Investigational medicinal product name	placebo suppository
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suppository
Routes of administration	Rectal use

Dosage and administration details:

Arm C participants were given placebo suppositories twice a day (morning and evening) administered with the Sephure suppository applicator.

Number of subjects in period 1[1]	Arm A	Arm B	Arm C
Started	67	67	66
Completed	57	56	58
Not completed	10	11	8
Physician decision	1	3	2
Consent withdrawn by subject	1	1	2
Adverse event, non-fatal	4	2	3
Randomization problem	-	1	-
Pregnancy	-	-	1
geopolitical tension	1	-	-
Lost to follow-up	1	4	-
Protocol deviation	2	-	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The pre-assignment period (screening) included 784 subjects. The baseline period (dosing) included 200 randomized subjects.

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Arm A participants were given hydrocortisone acetate 90 mg suppositories twice a day.	
Reporting group title	Arm B
Reporting group description:	
Arm B participants were only given hydrocortisone acetate 90 mg suppositories once a day.	
Reporting group title	Arm C
Reporting group description:	
Arm C participants were only given a placebo suppository.	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	67	67	66
Age categorical Units: Subjects			

Age continuous			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: years arithmetic mean standard deviation	 45.3 ± 19.76	 41.0 ± 18.80	 41.0 ± 19.73
Gender categorical			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: Subjects			
Female	37	37	35
Male	30	30	31

Reporting group values	Total		
Number of subjects	200		
Age categorical Units: Subjects			

Age continuous			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: years arithmetic mean standard deviation	 -		
Gender categorical			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic			

outputs are provided for the mITT Set.			
Units: Subjects			
Female	109		
Male	91		

Subject analysis sets

Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

The Safety Set includes all randomized subjects who received at least one dose of study treatment. Subjects were included in the analysis according to the treatment received.

Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis Set includes all randomized subjects following the principle of intent-to-treat (ITT).

Subject analysis set title	ITT Analysis
Subject analysis set type	Intention-to-treat

Subject analysis set description:

The ITT Set includes all randomized subjects who were randomized using the IRT system.

Subject analysis set title	Modified ITT
Subject analysis set type	Modified intention-to-treat

Subject analysis set description:

The mITT Set includes all subjects in the ITT Set who did not have endocrinology intercurrent events

Reporting group values	Safety Set	Full Analysis Set	ITT Analysis
Number of subjects	200	200	199
Age categorical Units: Subjects			

Age continuous			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: years arithmetic mean standard deviation	 ±	 43.1 ± 14.90	 ±
Gender categorical			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: Subjects			
Female		109	
Male		91	

Reporting group values	Modified ITT		
Number of subjects	174		
Age categorical Units: Subjects			

Age continuous			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: years arithmetic mean standard deviation	±		
Gender categorical			
As the ITT population differs from the FAS by only a single subject and the Safety Set differs from the FAS by the treatment attribution of a single subject, tabular summaries of the demographics and baseline characteristics in these analysis sets have not been prepared. Additionally, no programmatic outputs are provided for the mITT Set.			
Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description:	
Arm A participants were given hydrocortisone acetate 90 mg suppositories twice a day.	
Reporting group title	Arm B
Reporting group description:	
Arm B participants were only given hydrocortisone acetate 90 mg suppositories once a day.	
Reporting group title	Arm C
Reporting group description:	
Arm C participants were only given a placebo suppository.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Set includes all randomized subjects who received at least one dose of study treatment. Subjects were included in the analysis according to the treatment received.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set includes all randomized subjects following the principle of intent-to-treat (ITT).	
Subject analysis set title	ITT Analysis
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT Set includes all randomized subjects who were randomized using the IRT system.	
Subject analysis set title	Modified ITT
Subject analysis set type	Modified intention-to-treat
Subject analysis set description:	
The mITT Set includes all subjects in the ITT Set who did not have endocrinology intercurrent events	

Primary: Primary Efficacy Variable

End point title	Primary Efficacy Variable
End point description:	
proportion of subjects with clinical remission at the End of Treatment visit (Day 29). Clinical remission is defined as the Modified Mayo Score of 0 to 2, with stool frequency subscore of 0 or 1 (minimum 1 point decrease from a Baseline score of 1 or 2), rectal bleeding subscore of 0, and endoscopic subscore of 0 or 1.	
End point type	Primary
End point timeframe:	
29 days	

End point values	Arm A	Arm B	Arm C	ITT Analysis
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	67	66	66	199
Units: 0-8	67	66	66	199

Statistical analyses

Statistical analysis title	Primary Endpoint - End of Treatment

Statistical analysis description:

A logistic regression model in which treatment, sex, concomitant ulcerative colitis medication use (user vs. nonuser), and geographical region are included as covariate terms (and remain in the model regardless of their significance) was used for the primary analysis.

Comparison groups	Arm A v Arm C
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0105
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	8.9331
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.3126
upper limit	60.7941

Statistical analysis title	Primary Endpoint - End of Treatment

Statistical analysis description:

A logistic regression model in which treatment, sex, concomitant ulcerative colitis medication use (user vs. nonuser), and geographical region are included as covariate terms (and remain in the model regardless of their significance) was used for the primary analysis.

Comparison groups	Arm B v Arm C
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0061
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	10.2893
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.5305
upper limit	69.1744

Secondary: Secondary Efficacy Variable - Rectal Bleeding

End point title	Secondary Efficacy Variable - Rectal Bleeding

End point description:

The following secondary endpoint was evaluated hierarchically with Baseline (Day 1) compared to End of Treatment (Day 29) and then Follow-up (Day 15):
• proportion of subjects with a rectal bleeding subscore of 0.
The secondary endpoints were evaluated as measured by the Modified Mayo Score according to the following:
• Change in rectal bleeding from Baseline (Day 1) to End of Treatment (Day 29).

• Change in rectal bleeding from Baseline (Day 1) to Follow-up (Day 15).

End point type	Secondary

End point timeframe:

29 days

End point values	Arm A	Arm B	Arm C	ITT Analysis
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	67	66	66	199
Units: 0-3	67	66	66	199

Statistical analyses

Statistical analysis title	Secondary - Rectal Bleeding, End of treatment B/C

Statistical analysis description:

The secondary efficacy endpoints were evaluated using the same logistic regression test as the primary efficacy analysis. Odds ratios and risk differences with two-sided 97.5% confidence intervals are reported with the placebo group as the reference group. The proportions of subjects in each HCA 90 mg Suppository treatment group meeting the criteria defined were also compared with placebo using a one-sided Fisher Exact Test, similar to the primary efficacy analysis.

Comparison groups	Arm B v Arm C
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.082
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.831
upper limit	14.106

Statistical analysis title	Secondary - Rectal Bleeding Follow- up B/C

Statistical analysis description:

The secondary efficacy endpoints were evaluated using the same logistic regression test as the primary efficacy analysis. Odds ratios and risk differences with two-sided 97.5% confidence intervals are reported with the placebo group as the reference group. The proportions of subjects in each HCA 90 mg Suppository treatment group meeting the criteria defined were also compared with placebo using a one-sided Fisher Exact Test, similar to the primary efficacy analysis.

Comparison groups	Arm B v Arm C

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0107
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	3.176
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.151
upper limit	8.761

Statistical analysis title	Secondary - Rectal Bleeding, End of treatment A/C
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.836
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	2.098
upper limit	16.232

Statistical analysis title	Secondary - Rectal Bleeding Follow- up A/C
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0456
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.524
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.894
upper limit	7.13

Secondary: Secondary Efficacy Variable - Reduction in Stool Frequency

End point title	Secondary Efficacy Variable - Reduction in Stool Frequency

End point description:

The following secondary endpoint was evaluated hierarchically with Baseline (Day 1) compared to End of Treatment (Day 29) and then Follow-up (Day 15):
• proportion of subjects with a reduction of stool frequency. Treatment response was defined as a score of 0 or 1, with at least a 1-point decrease from Baseline (Day 1)
The secondary endpoints were evaluated as measured by the Modified Mayo Score according to the following:
• Change in stool frequency from Baseline (Day 1) to End of Treatment (Day 29).
• Change in stool frequency from Baseline (Day 1) to Follow-up (Day 15).

End point type	Secondary

End point timeframe:

29 days

End point values	Arm A	Arm B	Arm C	ITT Analysis
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	67	66	66	199
Units: 0-3	67	66	66	199

Statistical analyses

Statistical analysis title	Secondary - Stool Frequency, End of treatment B/C

Statistical analysis description:

The secondary efficacy endpoints were evaluated using the same logistic regression test as the primary efficacy analysis. Odds ratios and risk differences with two-sided 97.5% confidence intervals are reported with the placebo group as the reference group. The proportions of subjects in each HCA 90 mg Suppository treatment group meeting the criteria defined were also compared with placebo using a one-sided Fisher Exact Test, similar to the primary efficacy analysis

Comparison groups	Arm B v Arm C
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0523
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.007
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.898
upper limit	4.486

Statistical analysis title	Secondary - Stool Frequency, Follow up B/C

Statistical analysis description:

The secondary efficacy endpoints were evaluated using the same logistic regression test as the primary efficacy analysis. Odds ratios and risk differences with two-sided 97.5% confidence intervals are

reported with the placebo group as the reference group. The proportions of subjects in each HCA 90 mg Suppository treatment group meeting the criteria defined were also compared with placebo using a one-sided Fisher Exact Test, similar to the primary efficacy analysis.

Comparison groups	Arm B v Arm C
Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0802
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.903
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.835
upper limit	4.337

Statistical analysis title	Secondary - Stool Frequency, End of treatment A/C
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1728
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.631
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.73
upper limit	3.646

Statistical analysis title	Secondary - Stool Frequency, Follow up A/C
Comparison groups	Arm A v Arm C
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.679
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	0.72
upper limit	3.912

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse events were reported from time of subject screening (24 September 2020) and recruitment until end of trial (19 September 2024).	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Arm B
Reporting group description: -	
Reporting group title	Arm A
Reporting group description: -	
Reporting group title	Arm C
Reporting group description: -	

Serious adverse events	Arm B	Arm A	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 67 (0.00%)	0 / 67 (0.00%)	0 / 66 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Arm B	Arm A	Arm C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 67 (13.43%)	10 / 67 (14.93%)	8 / 66 (12.12%)
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 67 (0.00%)	2 / 67 (2.99%)	0 / 66 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 67 (1.49%)	2 / 67 (2.99%)	3 / 66 (4.55%)
occurrences (all)	1	2	4
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	0 / 67 (0.00%)	2 / 67 (2.99%)	2 / 66 (3.03%)
occurrences (all)	0	2	2
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 67 (0.00%)	2 / 67 (2.99%)	0 / 66 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	2 / 67 (2.99%)	2 / 67 (2.99%)	2 / 66 (3.03%)
occurrences (all)	2	3	2
Flatulence			
subjects affected / exposed	3 / 67 (4.48%)	2 / 67 (2.99%)	0 / 66 (0.00%)
occurrences (all)	3	3	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 67 (0.00%)	2 / 67 (2.99%)	2 / 66 (3.03%)
occurrences (all)	0	2	2
Renal and urinary disorders			
Leukocyturia			
subjects affected / exposed	1 / 67 (1.49%)	2 / 67 (2.99%)	0 / 66 (0.00%)
occurrences (all)	1	3	0
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 67 (2.99%)	1 / 67 (1.49%)	0 / 66 (0.00%)
occurrences (all)	2	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 September 2021	Amendment to screening period and laboratory testing.
09 May 2022	Amendment to endoscopy screening procedure.
18 July 2023	Removal of interim analyses, and amendment to statistical analyses, diary, scoring inclusion, and screening procedures.
08 September 2023	Amendment to statistical analyses and DMC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported