Clinical trial results:
A randomized, double blind, placebo controlled, parallel group, multiple dose, induction study to evaluate the safety, tolerability and optimal dose of ABX464 compared with placebo in patients with moderate to severe ulcerative colitis who have inadequate response, loss of response, or intolerance with at least one of the following agents: immunosuppressant treatment (i.e. azathioprine, 6-mercaptopurine, methotrexate), tumor necrosis factor alpha [TNF-] inhibitors, vedolizumab, JAK inhibitors and/or corticosteroid treatment.

Summary

EudraCT number	2018-003558-26
Trial protocol	FR SI CZ DE SK HU PL BE GB IT
Global end of trial date	31 August 2022

Results information

Result version number	v1 (current)
This version publication date	20 February 2023
First version publication date	20 February 2023

Trial information

Trial identification

Sponsor protocol code	ABX464-103

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03760003
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ABIVAX
Sponsor organisation address	7-11 Boulevard Haussmann, Paris, France, 75009
Public contact	Clinical Operations, Abivax, +33 15383 0961, Paul.Gineste@abivax.com
Scientific contact	Clinical Operations, Abivax, +33 15383 0961, Paul.Gineste@abivax.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	31 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2021
Global end of trial reached?	Yes
Global end of trial date	31 August 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to determine an optimal ABX464 dose to be used in moderate to severe active ulcerative colitis patients who have failed or are intolerant to immunomodulators, Anti-TNFα, vedolizumab, JAK inhibitors and/or corticosteroids by comparing the mean change from baseline in the MMS at week 8 between each ABX464 group and placebo.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form (ICF)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 May 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	52 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 70
Country: Number of subjects enrolled	Slovakia: 18
Country: Number of subjects enrolled	Slovenia: 3
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Austria: 6
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Czechia: 14
Country: Number of subjects enrolled	France: 31
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 22
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Serbia: 5
Country: Number of subjects enrolled	Ukraine: 32
Country: Number of subjects enrolled	United States: 2

Worldwide total number of subjects	254
EEA total number of subjects	210

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)	239
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 355 patients were enrolled in the study. Of these, 101 patients were screen failures and 1 patient was a Baseline failure (the patient signed informed consent but withdrew before the baseline visit).

Period 1

Period 1 title	Randomized phase (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	Placebo

Arm description:

2 capsules of Placebo

Arm type	Placebo
Investigational medicinal product name	placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

once daily during a meal with a glass of water

Arm title	25mg ABX464

Arm description:

1 capsule of 25mg ABX464 + 1 capsule of Placebo

Arm type	Experimental
Investigational medicinal product name	obefazimod
Investigational medicinal product code	ABX464
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water.

Arm title	50mg ABX464

Arm description:

1 capsule of 50mg ABX464 + 1 capsule of Placebo

Arm type	Experimental
Investigational medicinal product name	obefazimod
Investigational medicinal product code	ABX464
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water

Arm title	100mg ABX464

Arm description:

2 capsules of 50mg ABX464

Arm type	Experimental
Investigational medicinal product name	obefazimod
Investigational medicinal product code	ABX464
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Depending on the randomization, patients will be treated with a daily dose of either 25mg, 50mg or 100mg of ABX464 or matching placebo. All patients regardless of the treatment group will receive 2 capsules every day.
Patients will be orally dosed in a fed condition (regular meal) in the morning with a glass of water.

Number of subjects in period 1	Placebo	25mg ABX464	50mg ABX464
Started	64	63	63
FAS	64	61	63
Completed	57	58	53
Not completed	7	5	10
Consent withdrawn by subject	2	-	3
Physician decision	-	1	-
Adverse event, non-fatal	4	1	6
Pregnancy	-	2	-
Lost to follow-up	-	-	1
Lack of efficacy	1	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	100mg ABX464
Started	64
FAS	64
Completed	54
Not completed	10
Consent withdrawn by subject	5

Physician decision	-
Adverse event, non-fatal	5
Pregnancy	-
Lost to follow-up	-
Lack of efficacy	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
2 capsules of Placebo	
Reporting group title	25mg ABX464
Reporting group description:	
1 capsule of 25mg ABX464 + 1 capsule of Placebo	
Reporting group title	50mg ABX464
Reporting group description:	
1 capsule of 50mg ABX464 + 1 capsule of Placebo	
Reporting group title	100mg ABX464
Reporting group description:	
2 capsules of 50mg ABX464	

Reporting group values	Placebo	25mg ABX464	50mg ABX464
Number of subjects	64	63	63
Age categorical Units: Subjects			
Adults (18-64 years)	60	58	60
From 65-84 years	4	5	3
Age continuous			
Age (years)			
Units: years			
arithmetic mean	41.1	41.5	40.2
standard deviation	± 14.43	± 14.16	± 13.94
Gender categorical Units: Subjects			
Female	24	22	36
Male	40	41	27

Reporting group values	100mg ABX464	Total	
Number of subjects	64	254	
Age categorical Units: Subjects			
Adults (18-64 years)	61	239	
From 65-84 years	3	15	
Age continuous			
Age (years)			
Units: years			
arithmetic mean	42.2		
standard deviation	± 12.34	-	

Gender categorical Units: Subjects			
Female	23	105	
Male	41	149	

Subject analysis sets

Subject analysis set title	Full analysis set [FAS]
Subject analysis set type	Full analysis

Subject analysis set description:

The FAS contained all patients included in the study who had received at least 1 dose of the study treatment, and who had Baseline data for at least 1 efficacy variable.

Reporting group values	Full analysis set [FAS]		
Number of subjects	252		
Age categorical Units: Subjects			
Adults (18-64 years)	237		
From 65-84 years	15		
Age continuous			
Age (years)			
Units: years			
arithmetic mean	41.2		
standard deviation	± 13.67		
Gender categorical Units: Subjects			
Female	104		
Male	148		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
2 capsules of Placebo	
Reporting group title	25mg ABX464
Reporting group description:	
1 capsule of 25mg ABX464 + 1 capsule of Placebo	
Reporting group title	50mg ABX464
Reporting group description:	
1 capsule of 50mg ABX464 + 1 capsule of Placebo	
Reporting group title	100mg ABX464
Reporting group description:	
2 capsules of 50mg ABX464	
Subject analysis set title	Full analysis set [FAS]
Subject analysis set type	Full analysis
Subject analysis set description:	
The FAS contained all patients included in the study who had received at least 1 dose of the study treatment, and who had Baseline data for at least 1 efficacy variable.	

Primary: Reduction from Baseline in MMS at Week 8.

End point title	Reduction from Baseline in MMS at Week 8.
End point description:	
Change from baseline to week 8	
End point type	Primary
End point timeframe:	
Week 8	

End point values	Placebo	25mg ABX464	50mg ABX464	100mg ABX464
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	60	59	54	58
Units: Least squares mean				
least squares mean (confidence interval 95%)	-1.9 (-2.4 to -1.5)	-3.1 (-3.6 to -2.6)	-3.2 (-3.7 to -2.7)	-2.9 (-3.4 to -2.5)

Statistical analyses

Statistical analysis title	ANCOVA MODEL PLACEBO vs ABX464 25 mg
Comparison groups	Placebo v 25mg ABX464
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANCOVA

Statistical analysis title	ANCOVA MODEL PLACEBO vs ABX464 50 mg
Comparison groups	Placebo v 50mg ABX464
Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANCOVA

Statistical analysis title	ANCOVA MODEL PLACEBO vs ABX464 100 mg
Comparison groups	100mg ABX464 v Placebo
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	ANCOVA

Secondary: CLINICAL RESPONSE	
End point title	CLINICAL RESPONSE
End point description: Number of patients with clinical response at week 8	
End point type	Secondary
End point timeframe: Week 8	

End point values	Placebo	25mg ABX464	50mg ABX464	100mg ABX464
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	61	63	64
Units: Number				
clinical reponse	22	38	37	32

End point values	Full analysis set [FAS]			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Number				
clinical reponse	129			

Statistical analyses

No statistical analyses for this end point

Secondary: CLINICAL REMISSION

End point title	CLINICAL REMISSION
End point description: Number of patients in clinical remission at week 8	
End point type	Secondary
End point timeframe: Week 8	

End point values	Placebo	25mg ABX464	50mg ABX464	100mg ABX464
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	61	63	64
Units: Number of patients				
Clinical remission	8	16	11	16

End point values	Full analysis set [FAS]			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Number of patients				
Clinical remission	51			

Statistical analyses

Statistical analysis title	Mantel-Haenszel Chi Square Test
Comparison groups	100mg ABX464 v 50mg ABX464 v 25mg ABX464 v Placebo v Full analysis set [FAS]

Number of subjects included in analysis	504
Analysis specification	Pre-specified
Analysis type	superiority
P-value	≥ 0.5
Method	Mantel-Haenszel

Secondary: ENDOSCOPIC IMPROVEMENT

End point title	ENDOSCOPIC IMPROVEMENT
End point description: Number of patients with endoscopic improvement	
End point type	Secondary
End point timeframe: Week 8	

End point values	Placebo	25mg ABX464	50mg ABX464	100mg ABX464
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	61	63	64
Units: Number of patients				
Endoscopic Improvement	8	20	21	24

End point values	Full analysis set [FAS]			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Number of patients				
Endoscopic Improvement	73			

Statistical analyses

No statistical analyses for this end point

Secondary: ENDOSCOPIC REMISSION

End point title	ENDOSCOPIC REMISSION
End point description: Number of patients with endoscopic remission	
End point type	Secondary
End point timeframe: Week 8	

End point values	Placebo	25mg ABX464	50mg ABX464	100mg ABX464
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	61	63	64
Units: Number of patients				
Endoscopic Remission	5	4	5	2

End point values	Full analysis set [FAS]			
Subject group type	Subject analysis set			
Number of subjects analysed	252			
Units: Number of patients				
Endoscopic Remission	16			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

OVERALL

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Safety Analysis Set (SAF): Placebo treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

Reporting group title	100 mg

Reporting group description:

Safety Analysis Set (SAF): 100 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

Reporting group title	50 mg

Reporting group description:

Safety Analysis Set (SAF): 50 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

Reporting group title	25 mg

Reporting group description:

Safety Analysis Set (SAF): 25 mg ABX464 treatment group
The SAF included all randomized patients who received at least 1 dose of the study treatment. If there was any doubt whether a patient was treated or not, they were assumed treated for the purposes of analysis. The SAF was used for all safety analyses and patients were analyzed as treated.

Serious adverse events	Placebo	100 mg	50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 64 (6.25%)	4 / 64 (6.25%)	4 / 63 (6.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (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
Myocardial infarction			

subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	3 / 64 (4.69%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	25 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 62 (1.61%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			

subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo	100 mg	50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 64 (46.88%)	45 / 64 (70.31%)	38 / 63 (60.32%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Rectal adenocarcinoma			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Hypertension			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Hypotension			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	2 / 63 (3.17%)
occurrences (all)	0	1	2
Fatigue			
subjects affected / exposed	0 / 64 (0.00%)	2 / 64 (3.13%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Pain			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Mite allergy			

subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Breast cyst			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Affective disorder			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Suicidal ideation			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0

Investigations			
Prothrombin time prolonged			
subjects affected / exposed	2 / 64 (3.13%)	1 / 64 (1.56%)	2 / 63 (3.17%)
occurrences (all)	2	1	2
C-reactive protein increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	2 / 63 (3.17%)
occurrences (all)	0	1	2
Lipase increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 64 (0.00%)	2 / 64 (3.13%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Glutamate dehydrogenase increased			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Neutrophil count increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
White blood cell count increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Blood cholesterol increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Blood fibrinogen decreased			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Blood fibrinogen increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Haematocrit decreased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Human chorionic gonadotropin increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Intraocular pressure increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Prostatic specific antigen increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Troponin I increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Troponin increased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1

Troponin T increased			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	2	0	0
Congestive cardiomyopathy			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Left ventricular hypertrophy			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Myocardial infarction			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 64 (7.81%)	27 / 64 (42.19%)	19 / 63 (30.16%)
occurrences (all)	5	29	21
Burning sensation			
subjects affected / exposed	0 / 64 (0.00%)	2 / 64 (3.13%)	0 / 63 (0.00%)
occurrences (all)	0	2	0
Migraine			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Syncope			

subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Dysgeusia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Facial paralysis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Peripheral sensorimotor neuropathy			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 64 (3.13%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	2	1	1
Iron deficiency anaemia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Thrombocytopenia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Eczema eyelids			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 64 (6.25%)	9 / 64 (14.06%)	4 / 63 (6.35%)
occurrences (all)	4	9	5
Abdominal pain upper			
subjects affected / exposed	0 / 64 (0.00%)	4 / 64 (6.25%)	3 / 63 (4.76%)
occurrences (all)	0	4	4
Colitis ulcerative			
subjects affected / exposed	4 / 64 (6.25%)	1 / 64 (1.56%)	4 / 63 (6.35%)
occurrences (all)	4	1	4
Vomiting			
subjects affected / exposed	1 / 64 (1.56%)	5 / 64 (7.81%)	2 / 63 (3.17%)
occurrences (all)	1	5	2
Proctalgia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 64 (0.00%)	2 / 64 (3.13%)	1 / 63 (1.59%)
occurrences (all)	0	2	1
Constipation			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	1	1	1
Abdominal distension			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	1	0	1
Faeces discoloured			

subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Frequent bowel movements			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Gastritis erosive			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Intestinal fistula			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Intestinal polyp			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Melaena			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Odynophagia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Pancreatitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Rectal haemorrhage			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	1	1	0
Hepatobiliary disorders			
Cholelithiasis migration			

subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Liver disorder			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Liver injury			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 64 (1.56%)	2 / 64 (3.13%)	0 / 63 (0.00%)
occurrences (all)	1	2	0
Skin lesion			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	2 / 63 (3.17%)
occurrences (all)	0	2	2
Rash			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	1 / 63 (1.59%)
occurrences (all)	0	1	1
Erythema nodosum			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Ingrowing nail			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Pityriasis rosea			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Skin mass			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1

Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Renal colic			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 64 (4.69%)	5 / 64 (7.81%)	1 / 63 (1.59%)
occurrences (all)	3	6	1
Myalgia			
subjects affected / exposed	0 / 64 (0.00%)	5 / 64 (7.81%)	0 / 63 (0.00%)
occurrences (all)	0	5	0
Back pain			
subjects affected / exposed	0 / 64 (0.00%)	3 / 64 (4.69%)	0 / 63 (0.00%)
occurrences (all)	0	3	0
Coccydynia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Osteoporosis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Pain in jaw			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0

Tendon disorder			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	3 / 63 (4.76%)
occurrences (all)	0	1	3
COVID-19			
subjects affected / exposed	2 / 64 (3.13%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	2	0	1
Oral herpes			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	1	1	0
Anal abscess			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Appendicitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Dermatophytosis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Herpes virus infection			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			

subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Pyoderma			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Tonsillitis			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 64 (0.00%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	1	1	0
Folate deficiency			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 64 (1.56%)	1 / 64 (1.56%)	0 / 63 (0.00%)
occurrences (all)	1	1	0

Dehydration			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Fluid retention			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0
Hyperlipasaemia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 64 (0.00%)	0 / 64 (0.00%)	1 / 63 (1.59%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	1 / 64 (1.56%)	0 / 64 (0.00%)	0 / 63 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	25 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 62 (53.23%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Rectal adenocarcinoma			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Hypotension			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Mite allergy			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Breast cyst			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Dysmenorrhoea			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Haemorrhagic ovarian cyst			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Dyspnoea			

subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Affective disorder			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Suicidal ideation			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Investigations			
Prothrombin time prolonged			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Alanine aminotransferase increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Glutamate dehydrogenase increased			

subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Neutrophil count increased				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
White blood cell count increased				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Blood cholesterol increased				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Blood fibrinogen decreased				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Blood fibrinogen increased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Blood lactate dehydrogenase increased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Haematocrit decreased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Haemoglobin decreased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Hepatic enzyme increased				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Human chorionic gonadotropin increased				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Intraocular pressure increased				

subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Liver function test increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Lymphocyte count decreased			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Prostatic specific antigen increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Troponin I increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Troponin increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Troponin T increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Congestive cardiomyopathy			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Left ventricular hypertrophy			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		

Myocardial infarction			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Palpitations			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Tachycardia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 62 (20.97%)		
occurrences (all)	14		
Burning sensation			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Facial paralysis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Parosmia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Restless legs syndrome			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Iron deficiency anaemia			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 62 (3.23%)		
occurrences (all)	2		
Eye disorders			
Eczema eyelids			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 62 (8.06%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	3 / 62 (4.84%)		
occurrences (all)	4		
Colitis ulcerative			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Proctalgia			

subjects affected / exposed	2 / 62 (3.23%)			
occurrences (all)	2			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Constipation				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences (all)	2			
Dyspepsia				
subjects affected / exposed	2 / 62 (3.23%)			
occurrences (all)	2			
Abdominal pain				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Abdominal distension				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Faeces discoloured				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Frequent bowel movements				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			
Gastritis erosive				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Intestinal fistula				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Intestinal polyp				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Melaena				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Odynophagia				

subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Pancreatitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
International normalised ratio increased			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Cholelithiasis migration			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Hepatic steatosis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Liver disorder			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Liver injury			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Rash			

subjects affected / exposed occurrences (all) Erythema nodosum subjects affected / exposed occurrences (all) Ingrowing nail subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) Pityriasis rosea subjects affected / exposed occurrences (all) Skin mass subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0 0 / 62 (0.00%) 0 1 / 62 (1.61%) 1 0 / 62 (0.00%) 0 0 / 62 (0.00%) 0 0 / 62 (0.00%) 0		
Renal and urinary disorders Chromaturia subjects affected / exposed occurrences (all) Renal colic subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0 0 / 62 (0.00%) 0		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all) Back pain	1 / 62 (1.61%) 1 0 / 62 (0.00%) 0		

subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Coccydynia			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Osteoporosis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Pain in jaw			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Tendon disorder			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
COVID-19			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 62 (1.61%)		
occurrences (all)	1		
Anal abscess			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		
Appendicitis			
subjects affected / exposed	0 / 62 (0.00%)		
occurrences (all)	0		

Cellulitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Dermatophytosis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Herpes virus infection				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Herpes zoster				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Pyoderma				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Respiratory tract infection				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	0 / 62 (0.00%)			
occurrences (all)	0			
Tooth abscess				
subjects affected / exposed	1 / 62 (1.61%)			
occurrences (all)	1			

Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	2 / 62 (3.23%) 2		
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1		
Folate deficiency subjects affected / exposed occurrences (all)	1 / 62 (1.61%) 1		
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Dehydration subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Fluid retention subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Hyperlipasaemia subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		
Iron deficiency subjects affected / exposed occurrences (all)	0 / 62 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 July 2019	Clinical response defined as reduction in Mayo score of greater than or equal to 3 points was changed to at least 2 points (Sections 2.0 and 8.2.2). For enrollment of patients in the study, moderately to severely active UC definition based on MMS range of 4 to 9 was modified to range 5 to 9 (Sections 2.0 and 9.3.1).
07 November 2019	Assessment of T3, T4 and TSH levels by local laboratory were added at Baseline, Day 57, Day 113 (Table 1).
12 December 2019	Addition of exclusion criterion: Patients who received live vaccine 30 days or fewer before first dose of study treatment and/or who is planning to receive such a vaccine during the study duration.
11 January 2020	US eligible patients were to be randomized only to once daily ABX464 50 mg, ABX464 25 mg, or placebo. US patients were not eligible to receive ABX464 100 mg once daily (Sections 9.1 and 9.4.3.1). Patients were required to have the following additional laboratory parameters obtained within 14 days prior to Baseline: creatinine clearance ≥90 mL min-1 by the Cockcroft-Gault equation within 60 days prior to baseline, fibrinogen >0.9 × lower limit of normal and international normalized ratio ≤1.2 (if no anticoagulant therapy) (Section 9.3.1). Prohibited concomitant medications were updated to include drugs that inhibit or induce CYP1A2 and drugs that inhibit UGTIA9 activity and inhibitors or substrates of OATP1B1/1B3 transporters (Section 9.4.5). Patients enrolled in the US were not rolled over an open label extension study (ABX464-104). Patients were to be treated for 16 weeks and an end of study visit was to be performed within a week after last dosing (Section 9.1).
01 June 2020	The definition of clinical remission (a secondary endpoint) was changed (Sections 2.0 and 8.2.2). Exclusion criterion added: patients who received live vaccine 30 days or fewer before first dose of study treatment and/or who is planning to receive such a vaccine during the study duration (Section 9.3.2). Prohibited concomitant medications were updated to include drugs that inhibit or induce CYP1A2 and drugs that inhibit UGTIA9 activity and inhibitors of OATP1B1/1B3 transporters (Section 9.4.5).
30 July 2020	Similar to AMEND 2, (dated 01 june 2020)
08 October 2020	Similar to AMEND 2, (dated 01 june 2020)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported