Clinical trial results:
A randomized, subject- and investigator-blinded, placebo-controlled, parallel group study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of QBW251 in patients with bronchiectasis

Summary

EudraCT number	2019-002840-26
Trial protocol	GB DE
Global end of trial date	21 June 2023

Results information

Result version number	v1
This version publication date	07 July 2024
First version publication date	07 July 2024

Trial information

Trial identification

Sponsor protocol code	CQBW251C12201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04396366
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	21 June 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 June 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the change on sputum bacterial colonization.
Note: Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

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	02 February 2021
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	United Kingdom: 14
Country: Number of subjects enrolled	Germany: 4
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	China: 21
Worldwide total number of subjects	42
EEA total number of subjects	7

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)	28
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All inclusion and exclusion criteria were checked at screening.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	QBW251 300 mg b.i.d

Arm description:

Participants received QBW251 300 mg orally, twice daily (b.i.d.), for 12 weeks.

Arm type	Experimental
Investigational medicinal product name	QBW251
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received QBW251 300 mg orally, twice daily (b.i.d.), for 12 weeks.

Arm title	Placebo

Arm description:

Participants received matching placebo, b.i.d., for 12 weeks.

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

Dosage and administration details:

Participants received matching placebo, b.i.d., for 12 weeks.

Number of subjects in period 1	QBW251 300 mg b.i.d	Placebo
Started	21	21
Completed	20	21
Not completed	1	0
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	QBW251 300 mg b.i.d
Reporting group description:	
Participants received QBW251 300 mg orally, twice daily (b.i.d.), for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo, b.i.d., for 12 weeks.	

Reporting group values	QBW251 300 mg b.i.d	Placebo	Total
Number of subjects	21	21	42
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	14	14	28
From 65-84 years	7	7	14
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	52.8	56.2	
standard deviation	± 15.80	± 12.96	-
Sex: Female, Male Units: participants			
Female	11	10	21
Male	10	11	21
Race/Ethnicity, Customized Units: Subjects			
Asian	11	10	21
White	10	11	21

End points

End points reporting groups

Reporting group title	QBW251 300 mg b.i.d
Reporting group description:	
Participants received QBW251 300 mg orally, twice daily (b.i.d.), for 12 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received matching placebo, b.i.d., for 12 weeks.	

Primary: Change from Baseline In Bacterial Load Colony-forming Units of Potentially Pathogenic Microorganisms in Sputum at Week 12

End point title	Change from Baseline In Bacterial Load Colony-forming Units of Potentially Pathogenic Microorganisms in Sputum at Week 12[1]
End point description:	
No statistical analysis was planned for this primary outcome.	
End point type	Primary
End point timeframe:	
Baseline, 12 weeks	

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 planned for this primary outcome measure.

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	19		
Units: CFU/mL				
arithmetic mean (standard deviation)	-0.192 (± 1.4621)	0.340 (± 1.6476)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Participants with Absence of any Colony-forming Units of Potentially Pathogenic Bacteria Sputum

End point title	Proportion of Participants with Absence of any Colony-forming Units of Potentially Pathogenic Bacteria Sputum
End point description:	
End point type	Secondary
End point timeframe:	
Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in Quality of Life Questionnaire for Bronchiectasis (QOL-B) (Respiratory Symptoms Domain)

End point title	Change from baseline in Quality of Life Questionnaire for Bronchiectasis (QOL-B) (Respiratory Symptoms Domain)

End point description:

The Quality of Life Questionnaire for Bronchiectasis (QOL-B) is a disease-specific questionnaire developed for non-cystic fibrosis bronchiectasis. It covers 8 dimensions: physical functioning, role functioning, emotional functioning, social functioning, vitality, treatment burden, health perceptions, and respiratory symptoms. Each dimension is scored separately on a scale of 0 to 100, and higher scores represent better outcomes. Only the respiratory symptoms domain score will be reported for this outcome measure. Errors have been identified for the Quality of Life Questionnaire for Bronchiectasis (QOL-B) outcome measure in the final CSR, which don´t allow us to report results at this time. The CSR is currently being amended, and results will be provided by November 2024.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: score				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Data to be provided by November 2024.

[3] - Data to be provided by November 2024.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Fibrinogen Plasma Concentration

End point title	Change from Baseline in Fibrinogen Plasma Concentration

End point description:

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	19		
Units: g/L				
arithmetic mean (standard deviation)	-0.193 (± 0.6278)	-0.127 (± 0.4828)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pre-bronchodilator Forced Vital Capacity (FVC)

End point title	Change from Baseline in Pre-bronchodilator Forced Vital Capacity (FVC)

End point description:

Errors have been identified for the Quality of Life Questionnaire for Bronchiectasis (QOL-B) outcome measure in the final CSR, which don´t allow us to report results at this time. The CSR is currently being amended, and results will be provided by November 2024.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: liters				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Data to be provided by November 2024.

[5] - Data to be provided by November 2024.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Pre-bronchodilator Forced Exploratory Volume in the First Second (FEV1)

End point title	Change from Baseline in Pre-bronchodilator Forced Exploratory Volume in the First Second (FEV1)

End point description:

Errors have been identified for the Quality of Life Questionnaire for Bronchiectasis (QOL-B) outcome

measure in the final CSR, which don´t allow us to report results at this time. The CSR is currently being amended, and results will be provided by November 2024.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: liters				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - Data to be provided by November 2024.

[7] - Data to be provided by November 2024.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Rescue Medication Use (Salbutamol/Albuterol)

End point title	Change from Baseline in Rescue Medication Use (Salbutamol/Albuterol)

End point description:

Data were collected as the number of puffs taken at every 12-hour window. The first 12 hours of the day were categorized as "Morning" and the next 12 hours as "Evening". Total daily number of puffs was derived for each 24-hour window (per day), which was then used to calculate weekly and monthly average number of puffs taken. Baseline rescue medication use was defined as the average number of puffs per day in the screening period and the morning record at Day 1.

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	20		
Units: number of puffs				
arithmetic mean (standard deviation)	-0.37 (± 1.069)	0.14 (± 0.895)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Bronchus Area with Perimeter of 10 Millimeters

End point title	Change from Baseline in Bronchus Area with Perimeter of 10 Millimeters
End point description: Measured by high resolution computed tomography (HRCT)	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm				
arithmetic mean (standard deviation)				
Left Inferior Lobe Posterior Basal Segment n=21,21	-0.072 (± 0.3592)	-0.029 (± 1456)		
Left Superior Lobe Apical Segment n=16,18	-0.063 (± 0.4140)	0.029 (± 0.1600)		
Right Inferior Lobe Post. Basal Segment n=14,18	0.001 (± 0.1999)	-0.015 (± 0.1071)		
Right Middle Lobe Lateral Segment n=16,19	0.074 (± 0.1867)	0.039 (± 0.1471)		
Right Superior Lobe Apical Segment n=15,19	-0.037 (± 0.1990)	-0.026 (± 0.0991)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Mucus Score

End point title	Change from Baseline in Mucus Score
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: score				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	-0.9 (± 3.13)	-0.8 (± 1.68)		
Lung, Left Upper Lobe n=15,18	-0.9 (± 3.13)	-0.8 (± 1.63)		
Lung, Right Lower Lobe n=16,19	-0.9 (± 3.03)	-1.6 (± 3.83)		

Lung, Right Upper Lobe n=16,19	-0.9 (± 3.03)	-1.6 (± 3.83)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.9 (± 3.03)	-1.6 (± 3.83)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-0.9 (± 3.03)	-1.6 (± 3.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Region Percent Below or Equal to -856 Hounsfield units (HU)

End point title	Change from Baseline in Region Percent Below or Equal to -856 Hounsfield units (HU)

End point description:

The region percent below or equal to -856 HU represents air trapping, which was evaluated by HRCT in the whole lung and in the regions (thirds, lobes).

End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: change from baseline in % </= -856 HU				
arithmetic mean (standard deviation)				
Lung n=15,17	-0.284 (± 9.2755)	-1.074 (± 8.7794)		
Lung, Left n=15,17	-1.659 (± 8.5613)	-1.095 (± 7.2200)		
Lung, Left Lower Lobe n=15,17	-3.582 (± 8.4976)	-2.975 (± 7.8007)		
Lung, Left Upper Lobe n=15,17	0.002 (± 10.3698)	1.946 (± 10.7307)		
Lung, Right n=15,17	1.410 (± 10.8421)	-1.552 (± 10.1631)		
Lung, Right Lower Lobe n=15,17	0.303 (± 7.9933)	-2.193 (± 10.7784)		
Lung, Right Middle Lobe n=15,17	2.877 (± 10.3635)	0.502 (± 9.3885)		
Lung, Right Upper Lobe n=15,17	1.513 (± 13.1404)	-2.105 (± 11.4788)		
Thirds, Left Lower n=15,17	-2.726 (± 9.4063)	-1.109 (± 4.8754)		
Thirds, Left Middle n=15,17	-2.319 (± 8.3145)	-0.892 (± 8.0664)		
Thirds, Left Upper n=15,17	0.940 (± 10.8083)	-1.056 (± 9.7966)		
Thirds, Right Lower n=15,17	0.394 (± 9.2444)	-2.214 (± 9.6626)		

Thirds, Right Middle n=15,17	1.563 (± 11.7119)	-0.804 (± 10.4909)		
Thirds, Right Upper n=15,17	1.905 (± 12.7615)	-2.052 (± 11.7677)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Region Air Volume

End point title	Change from Baseline in Region Air Volume
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: liters				
arithmetic mean (standard deviation)				
Lung n=16,19	7.588 (± 362.231)	-4.667 (± 323.292)		
Lung, Left n=16,19	6.719 (± 188.304)	-7.304 (± 144.047)		
Lung, Left Lower Lobe n=15,19	22.142 (± 125.643)	-14.848 (± 84.4328)		
Lung, Left Upper Lobe n=16,19	-14.039 (± 82.9500)	7.545 (± 69.1768)		
Lung, Right n=16,19	0.869 (± 179.912)	2.637 (± 190.892)		
Lung, Right Lower Lobe n=16,19	9.886 (± 95.0629)	-5.435 (± 105.079)		
Lung, Right Middle Lobe n=16,19	-3.233 (± 20.4193)	1.242 (± 13.5834)		
Lung, Right Upper Lobe n=16,19	-5.784 (± 78.3195)	6.830 (± 81.4095)		
Thirds, Left Lower n=16,19	-3.409 (± 82.0621)	-5.155 (± 50.2945)		
Thirds, Left Middle n=16,19	-1.319 (± 76.6437)	-1.992 (± 63.8795)		
Thirds, Left Upper n=16,19	11.444 (± 73.0426)	-0.432 (± 41.7288)		
Thirds, Right Lower n=16,19	-20.490 (± 122.493)	-7.548 (± 76.9902)		
Thirds, Right Middle n=16,19	8.762 (± 98.3416)	2.994 (± 93.2434)		
Thirds, Right Upper n=16,19	12.574 (± 84.6939)	5.327 (± 60.5143)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Inner Area

End point title	Change from Baseline in Segment Average Inner Area
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm^2				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	2.009 (± 10.4977)	-1.376 (± 6.5410)		
Lung, Left Upper Lobe n=15,18	1.106 (± 11.1387)	1.506 (± 7.5668)		
Lung, Right Lower Lobe n=16,19	-0.677 (± 7.9904)	-2.119 (± 6.7263)		
Lung, Right Upper Lobe n=16,19	0.667 (± 4.9950)	-2.653 (± 14.9922)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	0.138 (± 4.8198)	-0.379 (± 2.8929)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-0.502 (± 5.2215)	1.828 (± 5.5992)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Major Inner Diameter

End point title	Change from Baseline in Segment Average Major Inner Diameter
End point description: Measured by HRCT	
End point type	Secondary

End point timeframe:
Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	0.364 (± 1.0234)	-0.128 (± 0.5242)		
Lung, Left Upper Lobe n=15,18	-0.095 (± 0.7972)	-0.116 (± 0.7192)		
Lung, Right Lower Lobe n=16,19	-0.040 (± 0.7883)	-0.207 (± 0.7876)		
Lung, Right Upper Lobe n=16,19	0.081 (± 0.7149)	-0.525 (± 1.9690)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	0.075 (± 0.9001)	-0.066 (± 0.5419)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	0.046 (± 0.8759)	0.336 (± 1.2354)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Minor Inner Diameter

End point title	Change from Baseline in Segment Average Minor Inner Diameter
End point description:	
Measured by HRCT	
End point type	Secondary
End point timeframe:	
Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	0.080 (± 0.8100)	-0.204 (± 0.7995)		
Lung, Left Upper Lobe n=15,18	0.160 (± 0.7449)	0.120 (± 0.5935)		
Lung, Right Lower Lobe n=16,19	-0.011 (± 0.6186)	-0.220 (± 0.6556)		

Lung, Right Upper Lobe n=16,19	0.034 (± 0.4546)	0.127 (± 0.5699)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.037 (± 0.5225)	-0.058 (± 0.4702)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-0.309 (± 0.7621)	0.065 (± 0.5016)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Outer Area

End point title	Change from Baseline in Segment Average Outer Area
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm^2				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	3.805 (± 15.3509)	-3.575 (± 9.6603)		
Lung, Left Upper Lobe n=15,18	2.527 (± 25.2783)	6.387 (± 15.1487)		
Lung, Right Lower Lobe n=16,19	-0.887 (± 13.2296)	-2.439 (± 10.4313)		
Lung, Right Upper Lobe n=16,19	3.054 (± 11.6503)	-6.171 (± 35.7465)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	0.011 (± 8.9779)	-0.574 (± 6.6601)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-1.929 (± 12.3065)	3.655 (± 9.0492)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Wall Area Fraction

End point title	Change from Baseline in Segment Average Wall Area Fraction
End point description: Measured by HRCT	
End point type	Secondary

End point timeframe:
Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: percent				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	-0.009 (± 0.0515)	-0.002 (± 0.0310)		
Lung, Left Upper Lobe n=15,18	0.002 (± 0.0553)	0.013 (± 0.0436)		
Lung, Right Lower Lobe n=16,19	0.001 (± 0.0377)	0.011 (± 0.0277)		
Lung, Right Upper Lobe n=16,19	0.007 (± 0.0392)	0.001 (± 0.0347)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.002 (± 0.0414)	0.006 (± 0.0262)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	0.007 (± 0.0281)	0.002 (± 0.0347)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Average Wall Thickness

End point title	Change from Baseline in Segment Average Wall Thickness
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	0.001 (± 0.1680)	-0.042 (± 0.0987)		
Lung, Left Upper Lobe n=15,18	0.014 (± 0.3422)	0.081 (± 0.2417)		
Lung, Right Lower Lobe n=16,19	0.001 (± 0.1691)	0.021 (± 0.0900)		

Lung, Right Upper Lobe n=16,19	0.054 (± 0.2231)	-0.030 (± 0.2941)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.014 (± 0.0828)	-0.004 (± 0.0968)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-0.040 (± 0.1606)	0.057 (± 0.0766)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Wall Area Percent

End point title	Change from Baseline in Segment Wall Area Percent
End point description: Measured by HRCT	
End point type	Secondary
End point timeframe: Baseline, 12 weeks	

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: percent				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	-0.009 (± 0.0515)	-0.002 (± 0.0305)		
Lung, Left Upper Lobe n=15,18	0.002 (± 0.0553)	0.013 (± 0.0437)		
Lung, Right Lower Lobe n=16,19	0.001 (± 0.0376)	0.011 (± 0.0276)		
Lung, Right Upper Lobe n=16,19	0.007 (± 0.0394)	0.002 (± 0.0337)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.003 (± 0.0411)	0.006 (± 0.0261)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	0.007 (± 0.0282)	0.002 (± 0.0347)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Segment Wall Area

End point title	Change from Baseline in Segment Wall Area
End point description: Measured by HRCT	
End point type	Secondary

End point timeframe:

Baseline, 12 weeks

End point values	QBW251 300 mg b.i.d	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	21		
Units: mm^2				
arithmetic mean (standard deviation)				
Lower Lobe Bronchus, Left n=15,17	1.796 (± 6.6301)	-2.199 (± 4.3938)		
Lung, Left Upper Lobe n=15,18	1.421 (± 18.5698)	4.881 (± 12.4380)		
Lung, Right Lower Lobe n=16,19	-0.209 (± 6.9730)	-0.320 (± 4.5446)		
Lung, Right Upper Lobe n=16,19	2.388 (± 9.7223)	-3.518 (± 21.8864)		
Lung, Right, Middle Lobe, Lateral Segment n=16,19	-0.127 (± 4.6312)	-0.194 (± 4.0452)		
Lung, Right, Middle Lobe, Medial Segment n=16,19	-1.427 (± 7.3051)	1.827 (± 3.8885)		

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of QBW251

End point title	Cmax of QBW251[8]

End point description:

Maximum (peak) plasma concentration of QBW251

End point type	Secondary

End point timeframe:

1h, 2h, 3h, 4h, 6h and 8h post-dose on Days 1 and 28, and 3h post-dose on Day 56 and Day 84

Notes:

[8] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 n=19	1120 (± 913)			
Day 28 n=19	1520 (± 951)			
Day 56 n=19	1190 (± 578)			
Day 84 n=18	1460 (± 947)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of QBW251

End point title	Ctrough of QBW251[9]

End point description:

Trough (pre-dose) plasma concentration of QBW251

End point type	Secondary

End point timeframe:

Pre-dose Day 1, Day 28, Day 56, Day 84

Notes:

[9] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1 n=21	0.00 (± 0.00)			
Day 28 n=20	489 (± 371)			
Day 56 n=19	483 (± 395)			
Day 84 n=18	498 (± 416)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of QBW251 for a Serial PK Set

End point title	Cmax of QBW251 for a Serial PK Set[10]

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

Notes:

[10] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1	2470 (± 787)			
Day 28	3000 (± 1390)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUClast of QBW251 for a Serial PK Set

End point title	AUClast of QBW251 for a Serial PK Set[11]

End point description:

Area under the concentration-time curve up to the last measurable concentration of QBW251 (AUClast)

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
Day 1	6100 (± 2340)			
Day 28	10300 (± 3100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of QBW251 for a Serial PK Set

End point title	Ctrough of QBW251 for a Serial PK Set[12]

End point description:

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

Notes:

[12] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: ng/mL				
arithmetic mean (standard deviation)				
Day 1	0.00 (± 0.00)			
Day 28	603 (± 142)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of QBW251 for a Serial PK Set

End point title	Tmax of QBW251 for a Serial PK Set[13]

End point description:

Time to reach maximum (peak) plasma concentration after single-dose administration

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

Notes:

[13] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hours				
median (full range (min-max))				
Day 1	1.00 (1.00 to 4.00)			
Day 28	2.00 (1.00 to 3.08)			

Statistical analyses

No statistical analyses for this end point

Secondary: AUC0-12h of QBW251 for a Serial PK Set

End point title	AUC0-12h of QBW251 for a Serial PK Set[14]

End point description:

Twelve-hour AUC

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

Notes:

[14] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: h*ng/mL				
arithmetic mean (standard deviation)				
Day 1 n=2 Day 28 n=1	5260 (± 1780) 15400 (± 999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Tlast of QBW251 for a Serial PK Set

End point title	Tlast of QBW251 for a Serial PK Set[15]

End point description:

Tlast is the last measurable concentration sampling time.

End point type	Secondary

End point timeframe:

Pre-dose, 1h, 2h, 3h, 4h, 6h and 8h post-dose on Day 1 and Day 28

Notes:

[15] - 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: Pharmacokinetic parameters were only analyzed for the QBW251 arm.

End point values	QBW251 300 mg b.i.d			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: hours				
arithmetic mean (standard deviation)				
Day 1 Day 28	7.99 (± 0.00962) 8.00 (± 0.00)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Treatment-emergent adverse events	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1
Reporting groups	
Reporting group title	QBW251 300 mg b.i.d
Reporting group description:	
QBW251 300 mg b.i.d	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Serious adverse events	QBW251 300 mg b.i.d	Total	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 21 (9.52%)	2 / 42 (4.76%)	0 / 21 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infective exacerbation of bronchiectasis			
subjects affected / exposed	1 / 21 (4.76%)	1 / 42 (2.38%)	0 / 21 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
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	QBW251 300 mg b.i.d	Total	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 21 (66.67%)	27 / 42 (64.29%)	13 / 21 (61.90%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 21 (14.29%)	3 / 42 (7.14%)	0 / 21 (0.00%)
occurrences (all)	3	3	0
Headache			
subjects affected / exposed	2 / 21 (9.52%)	4 / 42 (9.52%)	2 / 21 (9.52%)
occurrences (all)	2	4	2
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 21 (14.29%)	8 / 42 (19.05%)	5 / 21 (23.81%)
occurrences (all)	3	8	5
Peripheral swelling			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Pyrexia			
subjects affected / exposed	3 / 21 (14.29%)	4 / 42 (9.52%)	1 / 21 (4.76%)
occurrences (all)	3	4	1
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Respiratory, thoracic and mediastinal disorders			
Bronchiectasis			
subjects affected / exposed	8 / 21 (38.10%)	12 / 42 (28.57%)	4 / 21 (19.05%)
occurrences (all)	8	12	4
Cough			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	2 / 21 (9.52%)
occurrences (all)	0	2	2
Oropharyngeal pain			
subjects affected / exposed	0 / 21 (0.00%)	2 / 42 (4.76%)	2 / 21 (9.52%)
occurrences (all)	0	3	3
Rhinorrhoea			

subjects affected / exposed	1 / 21 (4.76%)	3 / 42 (7.14%)	2 / 21 (9.52%)
occurrences (all)	1	3	2
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 21 (14.29%)	4 / 42 (9.52%)	1 / 21 (4.76%)
occurrences (all)	3	4	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 21 (9.52%)	4 / 42 (9.52%)	2 / 21 (9.52%)
occurrences (all)	2	4	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2021	This protocol amendment: Clarified that the dose to be used in the study was 300 mg b.i.d, as well as the respective dose rationale; Removed the requirement for the serious adverse reactions to be similar in nature as a pre-requisite to put the study on hold; Included a statement that any restart following a temporary hold due to stopping rules being met would require the competent authorities and ethic committees' approval; Clarified the primary analysis strategy.
04 November 2021	This protocol amendment addressed the following changes: two inclusion and one exclusion criteria were amended to improve study feasibility and recruitment. These changes expanded the number of eligible participants but did not change the overall patient profile for the study.
02 December 2022	This protocol amendment: Removed the stopping rules for NOAEL threshold limits; Discontinued the DMC involvement in the trial; Clarified the requirement of participant's completion of the exacerbations of COPD Tool - Patient Reported Outcome (EXACT-PRO) during screening/baseline period for the purpose of EXACT-PRO baseline score calculation to correctly set up EXACT-PRO alert after patient's being randomized; Updated the exploratory objective and endpoints related to mucus burden to be more specific; Reduced the number of ECGs to one per visit; Updated the co-medication lists to include the most updated drug-drug interaction (DDI) information based on clinical DDI study (CQBW251A2107) and in vitro data; Clarified the inclusion/exclusion criteria, allowing patients with primary ciliary dyskinesia (PCD) to participate; Clarified inclusion criteria, including the use of screening HRCT to satisfy inclusion in the study and clarified that Haemophilus parainfluenzae alone was not permitted for inclusion as a pathogenic organism; Introduced flexibility in the number of attempts for spontaneous sputum collection for each visit before attempting induced sputum collection; Allowed participants at selected sites, upon approval of the sponsor, to forgo HRCT scanning.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: