



Clinical trial results:

A Phase 2, Multi-Centre, Open-Label, Single-Arm Trial Investigating the Safety, Efficacy and Pharmacokinetics of C21 in Subjects with Idiopathic Pulmonary Fibrosis

Summary

EudraCT number	2020-000822-24
Trial protocol	GB
Global end of trial date	30 March 2024

Results information

Result version number	v1 (current)
This version publication date	19 March 2025
First version publication date	19 March 2025

Trial information

Trial identification

Sponsor protocol code	VP-C21-005
-----------------------	------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04533022
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vicore Pharma AB
Sponsor organisation address	Kornhamnstorg 53, Stockholm, Sweden, SE-111 27
Public contact	Anne Katrine Cohrt, Vicore Pharma AB, anne-katrine.cohrt@vicorepharma.com
Scientific contact	Bertil Lindmark, Vicore Pharma AB, bertil.lindmark@vicorepharma.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	10 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2024
Global end of trial reached?	Yes
Global end of trial date	30 March 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the safety of C21 with 200 mg daily dose (100 mg b.i.d.) administered orally to subjects with IPF.

Protection of trial subjects:

None.

Background therapy:

None

Evidence for comparator: -

Actual start date of recruitment	13 November 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	United Kingdom: 7
Country: Number of subjects enrolled	India: 38
Country: Number of subjects enrolled	Ukraine: 4
Country: Number of subjects enrolled	Russian Federation: 3
Worldwide total number of subjects	52
EEA total number of subjects	0

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)	18
From 65 to 84 years	34

85 years and over	0
-------------------	---

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

One hundred and thirty-eight subjects provided informed consent and were enrolled in the trial; 86 of these subjects were screening failures. The remaining 52 subjects received at least one dose of IMP.

Period 1

Period 1 title	Trial period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	C21 100 mg BID
-----------	----------------

Arm description:

Oral capsules of C21 (buloxibutid) 100 mg administered twice daily (BID)

Arm type	Experimental
Investigational medicinal product name	C21
Investigational medicinal product code	
Other name	compound 21, buloxibutid
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg twice daily (BID) for 36 weeks

Number of subjects in period 1	C21 100 mg BID
Started	52
Completed	27
Not completed	25
Adverse event, serious fatal	2
Consent withdrawn by subject	15
FVC decline, FVCpp<60% and worsening of resp symp	1
Adverse event, non-fatal	5
FVC decline and FVCpp<60%	2

Baseline characteristics

Reporting groups

Reporting group title	Trial period
Reporting group description: -	

Reporting group values	Trial period	Total	
Number of subjects	52	52	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	18	
From 65-84 years	34	34	
85 years and over	0	0	
Age continuous			
Age at screening			
Units: years			
arithmetic mean	67.3		
standard deviation	± 9.38	-	
Gender categorical			
Units: Subjects			
Female	12	12	
Male	40	40	
Ethnic origin			
Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	52	52	
Race			
Units: Subjects			
Black or African American	0	0	
American Indian or Alaska Native	0	0	
Asian	38	38	
Native Hawaiian or Other Pacific Islander	0	0	
White	14	14	
Other	0	0	
Smoking status			
Units: Subjects			
Current	0	0	
Former	10	10	
Never	42	42	
E-cigarettes and vapes status			
Units: Subjects			

Current	0	0	
Former	1	1	
Never	51	51	
Previous use of antifibrotics			
Units: Subjects			
Nintedanib	0	0	
Pirfenidone	0	0	
Neither nintedanib or pirfenidone	52	52	
HRCT pattern (central reading)			
HRCT pattern (central reading)			
Units: Subjects			
Typical UIP HRCT Pattern	20	20	
Probable UIP HRCT	32	32	
Height			
Height at screening			
Units: cm			
arithmetic mean	161.7		
standard deviation	± 8.7	-	
Weight			
Weight at screening			
Units: kg			
arithmetic mean	64.6		
standard deviation	± 14.2	-	
BMI			
Body mass index (BMI) at screening			
Units: kg/m ²			
arithmetic mean	24.57		
standard deviation	± 4.12	-	
Time since diagnosis of IPF			
Units: Years			
arithmetic mean	1.01		
standard deviation	± 1.195	-	
Oxygen saturation at screening			
Units: percent			
arithmetic mean	95.3		
standard deviation	± 2.40	-	
FEV1			
Units: liters			
arithmetic mean	1.912		
standard deviation	± 0.528	-	
FVC			
Units: Liters			
arithmetic mean	2.387		
standard deviation	± 0.667	-	
FEV1 (% predicted normal)			
Units: Percent			
arithmetic mean	77.51		
standard deviation	± 14.687	-	
FVC (% predicted normal)			
Units: percent			
arithmetic mean	75.46		

standard deviation	± 13.662	-	
FEV1/FVC (ratio)			
Units: Ratio			
arithmetic mean	0.804		
standard deviation	± 0.0673	-	
Age of HRCT scans			
Units: Months			
arithmetic mean	5.58		
standard deviation	± 8.720	-	

End points

End points reporting groups

Reporting group title	C21 100 mg BID
Reporting group description:	
Oral capsules of C21 (buloxibutid) 100 mg administered twice daily (BID)	

Primary: Nature and frequency of adverse events occurring over the trial period

End point title	Nature and frequency of adverse events occurring over the trial period ^[1]
-----------------	---

End point description:

Adverse events were recorded from signing of informed consent until end of trial.

Nature and frequency of adverse events are presented in the adverse events section.

End point type	Primary
----------------	---------

End point timeframe:

From signing of informed consent until end of trial.

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: A statistical analysis has not been made on the safety data. More details on the safety data are provided in the Adverse event section.

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: Subjects				
Total number of subjects with TEAEs	37			
Total number of subjects with serious TEAEs	5			
Subjects with serious treatment-related TEAEs	0			
Total number of subjects with TEAEs leading to wi	6			
Total number of subjects with TEAEs leading to di	12			
Total number of subj. w. TEAEs leading to death	2			
Subjects with treatment-rel. TEAEs lead to disc.	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity (Non-imputed Data)

End point title	Change From Baseline in Forced Vital Capacity (Non-imputed Data)
-----------------	--

End point description:

End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-4.9 (-73.2 to 63.4)			
Week 24	16.0 (-117.4 to 149.3)			
Week 36	216.0 (36.9 to 395.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in forced vital capacity (imputed data)

End point title	Change from baseline in forced vital capacity (imputed data)
End point description:	
End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-57.6 (-123.3 to 8.1)			
Week 24	-70.3 (-170.5 to 29.9)			
Week 36	9.4 (-115.6 to 134.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity - FVC12AS (Imputed Data)

End point title	Change From Baseline in Forced Vital Capacity - FVC12AS (Imputed Data)
-----------------	--

End point description:

Mean changes in force vital capacity (mL) from baseline to Week 12, 24, and 36 were calculated for the FVC Week 12 analysis set (FVC12AS) (imputed data).

FVC12AS is the subset of subjects that had not withdrawn at Week 12.

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-6.6 (-71.3 to 58.0)			
Week 24	-5.2 (-121.1 to 110.7)			
Week 36	116.0 (-27.4 to 259.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity - FVC24AS (Imputed Data)

End point title	Change From Baseline in Forced Vital Capacity - FVC24AS (Imputed Data)
-----------------	--

End point description:

Mean changes in force vital capacity (mL) from baseline to Week 12, 24, and 36 were calculated for the FVC Week 24 analysis set (FVC24AS) (imputed data).

FVC24AS is the subset of subjects who had not withdrawn at Week 24.

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	0.6 (-67.2 to 68.3)			
Week 24	16.0 (-117.4 to 149.3)			
Week 36	165.5 (4.1 to 326.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Forced Vital Capacity - PPAS (Imputed Data)

End point title	Change From Baseline in Forced Vital Capacity - PPAS (Imputed Data)
End point description: Mean changes in force vital capacity (mL) from baseline to Week 12, 24, and 36 were calculated in the per protocol analysis set (PPAS)	
End point type	Secondary
End point timeframe: 36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-51.5 (-115.7 to 12.7)			
Week 24	-53.2 (-158.2 to 51.9)			
Week 36	33.1 (-98.6 to 164.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in forced vital capacity by subgroup, Week 12 (imputed data)

End point title	Change in forced vital capacity by subgroup, Week 12 (imputed
-----------------	---

	data)
End point description:	
End point type	Secondary
End point timeframe:	
12 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mL				
arithmetic mean (confidence interval 90%)				
Typical UIP	-107.9 (-241.3 to 25.4)			
Probable UIP	-27.5 (-100.1 to 45.1)			
India	-27.4 (-98.4 to 43.6)			
Rest of world	-139.0 (-298.0 to 20.0)			
FVC predicted normal ≤ 70%	4.8 (-78.1 to 87.7)			
FVC predicted normal: > 70%	-106.2 (-204.8 to -7.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced Vital Capacity by Subgroup, Week 24 (Imputed Data)

End point title	Change in Forced Vital Capacity by Subgroup, Week 24 (Imputed Data)
End point description:	
End point type	Secondary
End point timeframe:	
24 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mL				
arithmetic mean (confidence interval 90%)				

Typical UIP	-95.8 (-268.9 to 77.3)			
Probable UIP	-55.0 (-183.8 to 73.7)			
India	-44.8 (-165.9 to 76.3)			
Rest of world	-139.1 (-333.5 to 55.4)			
FVC predicted normal \leq 70%	-2.8 (-161.2 to 155.6)			
FVC predicted normal: > 70%	-122.8 (-256.8 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced Vital Capacity by Subgroup, Week 36 (Imputed Data)

End point title	Change in Forced Vital Capacity by Subgroup, Week 36 (Imputed Data)
End point description:	
End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: mL				
arithmetic mean (confidence interval 90%)				
Typical UIP	-161.1 (-338.4 to 16.2)			
Probable UIP	111.6 (-56.4 to 279.6)			
India	58.3 (-101.6 to 218.3)			
Rest of world	-122.5 (-300.9 to 55.9)			
FVC predicted normal: \leq 70%	58.1 (-98.4 to 214.6)			
FVC predicted normal: >70%	-28.6 (-221.4 to 164.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced Vital Capacity by Subgroup, Week 12 (non-Imputed Data)

End point title	Change in Forced Vital Capacity by Subgroup, Week 12 (non-Imputed Data)
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

12 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mL				
arithmetic mean (confidence interval 90%)				
Typical UIP	8.3 (-116.1 to 132.6)			
Probable UIP	-11.7 (-99.0 to 75.6)			
India	11.9 (-62.3 to 86.0)			
Rest of world	-53.3 (-235.3 to 128.6)			
FVC predicted normal ≤ 70%	3.0 (-91.3 to 97.3)			
FVC predicted normal: > 70%	-13.2 (-121.3 to 94.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced Vital Capacity by Subgroup, Week 24 (Non-Imputed Data)

End point title	Change in Forced Vital Capacity by Subgroup, Week 24 (Non-Imputed Data)
-----------------	---

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

24 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mL				
arithmetic mean (confidence interval 90%)				
Typical UIP	81.3 (-125.3 to 287.8)			
Probable UIP	-18.2 (-199.5 to 163.0)			
India	41.6 (-136.0 to 219.3)			
Rest of world	-40.5 (-249.2 to 168.2)			
FVC predicted normal ≤ 70%	40.3 (-181.8 to 262.4)			
FVC predicted normal: > 70%	-5.5 (-182.0 to 171.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced Vital Capacity by Subgroup, Week 36 (Non-Imputed Data)

End point title	Change in Forced Vital Capacity by Subgroup, Week 36 (Non-Imputed Data)
End point description:	
End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	28			
Units: mL				
arithmetic mean (confidence interval 90%)				
Typical UIP	27.2 (-216.3 to 270.7)			
Probable UIP	320.9 (73.0 to 568.8)			
India	276.5 (31.0 to 521.9)			
Rest of world	64.9 (-103.7 to 233.5)			
FVC predicted normal ≤ 70%	239.0 (-2.0 to 480.0)			

FVC predicted normal: > 70%	198.8 (-77.7 to 475.2)			
-----------------------------	------------------------	--	--	--

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of forced vital capacity decline over time, FAS

End point title	Rate of forced vital capacity decline over time, FAS
-----------------	--

End point description:

Mean Rates of forced vital capacity decline over time (mL) normalized to change over 24 weeks were calculated using a piece-wise linear regression model (non-imputed data).

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	50			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-8.2 (-141.9 to 125.5)			
Week 24	36.4 (-87.1 to 160.0)			
Week 36	108.9 (-4.8 to 222.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of forced vital capacity decline over time, FVC12AS

End point title	Rate of forced vital capacity decline over time, FVC12AS
-----------------	--

End point description:

Mean Rates of forced vital capacity decline over time (mL) normalized to change over 24 weeks were calculated in the FVC Week 12 analysis set (FVC12AS) using a Piece-wise Linear Regression Model (non-imputed data).

FVC12AS is the subset of subjects that had not withdrawn at Week 12.

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	37			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	25.1 (-140.7 to 190.8)			
Week 24	26.9 (-105.6 to 159.4)			
Week 36	113.9 (0.5 to 227.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of forced vital capacity decline over time, FVC24AS

End point title	Rate of forced vital capacity decline over time, FVC24AS
End point description:	
Mean Rates of forced vital capacity decline over time (mL) normalized to change over 24 weeks were calculated in the FVC Week 24 analysis set (FVC24AS) using a Piece-wise Linear Regression Model. FVC24AS is the subset of subjects that had not withdrawn at Week 24.	
End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	32			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	33.8 (-148.5 to 216.0)			
Week 24	46.4 (-98.6 to 191.3)			
Week 36	123.5 (7.9 to 239.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Forced expiratory volume in the first second (mL)

End point title Change in Forced expiratory volume in the first second (mL)

End point description:

Mean changes in FEV1 from baseline to 12, 24, and 36 weeks were calculated.

End point type Secondary

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: mL				
arithmetic mean (confidence interval 90%)				
Week 12	-34.1 (-91.3 to 23.2)			
Week 24	-24.8 (-115.5 to 65.8)			
Week 36	81.4 (-40.9 to 203.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of C21 evaluated in a subset of subjects, Day 1

End point title Plasma concentration of C21 evaluated in a subset of subjects,
Day 1

End point description:

Values below the LLOQ have been set to half the LLOQ (LLOQ = 10ng/mL).

End point type Secondary

End point timeframe:

Day 1

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
arithmetic mean (standard deviation)				
Prior to dosing	5.00 (\pm 0.00)			

30 min post dose	1622.00 (± 1453.64)			
1 h post dose	1788.11 (± 1112.484)			
2 h post dose	864.46 (± 1062.15)			
3 h post dose	322.19 (± 407.29)			
4 h post dose	282.82 (± 379.31)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of C21 evaluated in a sub-set of subjects, Week 12

End point title	Plasma Concentration of C21 evaluated in a sub-set of subjects, Week 12
End point description:	Values below the LLOQ have been set to half the LLOQ (LLOQ = 10ng/mL).
End point type	Secondary
End point timeframe:	12 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: ng/mL				
arithmetic mean (standard deviation)				
Prior to dosing	27.13 (± 62.58)			
30 min post dose	974.28 (± 1028.90)			
1 h post dose	1044.02 (± 1128.30)			
2 h post dose	794.02 (± 774.34)			
3 h post dose	491.25 (± 820.36)			
4 h post dose	101.50 (± 113.96)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of C21 Evaluated in a Sub-set of Subjects, Week 24

End point title	Plasma Concentration of C21 Evaluated in a Sub-set of Subjects, Week 24
-----------------	---

End point description:

Values below the LLOQ have been set to half the LLOQ (LLOQ = 10ng/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

24 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ng/mL				
arithmetic mean (standard deviation)				
Prior to dosing	20.14 (± 28.61)			
30 min post dose	615.53 (± 792.91)			
1 h post dose	898.61 (± 779.72)			
2 h post dose	404.80 (± 296.00)			
3 h post dose	151.30 (± 125.29)			
4 h post dose	115.93 (± 151.83)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of C21 Evaluated in a Sub-set of Subjects, Week 36

End point title	Plasma Concentration of C21 Evaluated in a Sub-set of Subjects, Week 36
-----------------	---

End point description:

Values below the LLOQ have been set to half the LLOQ (LLOQ = 10ng/mL).

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: ng/mL				
arithmetic mean (standard deviation)				
Prior to dosing	89.78 (± 176.45)			
30 min post dose	796.29 (± 839.35)			
1 h post dose	713.86 (± 453.54)			
2 h post dose	298.29 (± 299.24)			
3 h post dose	374.16 (± 459.55)			
4 h post dose	348.11 (± 479.79)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters in a Sub-set of Subjects, Cmax

End point title	PK Parameters in a Sub-set of Subjects, Cmax
End point description:	
End point type	Secondary
End point timeframe:	
36 weeks	

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Week 0	1852.13 (± 80.1)			
Week 12	954.29 (± 127.9)			
Week 24	524.79 (± 281.6)			
Week 36	961.86 (± 73.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters Evaluated in a Sub-set of Subjects, Tmax

End point title PK Parameters Evaluated in a Sub-set of Subjects, Tmax

End point description:

End point type Secondary

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: h				
median (full range (min-max))				
Week 0	1.00 (0.5 to 4.0)			
Week 12	1.50 (0.5 to 4.0)			
Week 24	1.00 (0.0 to 1.0)			
Week 36	1.00 (0.5 to 4.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters in a Sub-set of Subjects, AUClast

End point title PK Parameters in a Sub-set of Subjects, AUClast

End point description:

End point type Secondary

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: h*ng/mL)				
geometric mean (geometric coefficient of variation)				

Week 0	3018.15 (\pm 60.5)			
Week 12	1704.92 (\pm 126.6)			
Week 24	995.60 (\pm 213.2)			
Week 36	1622.77 (\pm 49.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameters in a Sub-set of Subjects, Accumulation ratio AUC

End point title	PK Parameters in a Sub-set of Subjects, Accumulation ratio AUC
-----------------	--

End point description:

End point type	Secondary
----------------	-----------

End point timeframe:

36 weeks

End point values	C21 100 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Ratio				
geometric mean (geometric coefficient of variation)				
Week 12	0.846 (\pm 120.5)			
Week 24	0.453 (\pm 328.9)			
Week 36	0.738 (\pm 67.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the trial from signing of informed consent until the end-of-trial visit, up to 44 weeks

Adverse event reporting additional description:

At each visit the subject was asked about AEs in an objective manner, e.g.: "Have you experienced any problems since the last visit?"

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	27.0
--------------------	------

Reporting groups

Reporting group title	C21 100 mg BID
-----------------------	----------------

Reporting group description: -

Serious adverse events	C21 100 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 52 (9.62%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Idiopathic pulmonary fibrosis			

subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Kidney infection			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Sepsis			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
COVID-19			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Type 2 diabetes			
subjects affected / exposed	1 / 52 (1.92%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	C21 100 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 52 (61.54%)		
Investigations			
Blood creatinine increased			
subjects affected / exposed	4 / 52 (7.69%)		
occurrences (all)	4		

C-reactive protein increased subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2		
Blood glucose increased subjects affected / exposed occurrences (all)	2 / 52 (3.85%) 2		
Alanine aminotransferase abnormal subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 3		
Aspartate aminotransferase abnormal subjects affected / exposed occurrences (all)	1 / 52 (1.92%) 2		
Cardiac disorders Bundle branch block left subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 3		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 8 3 / 52 (5.77%) 3		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all)	4 / 52 (7.69%) 4 1 / 52 (1.92%) 2		
Gastrointestinal disorders Gastro-oesophageal reflux disease			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 52 (7.69%)</p> <p>4</p> <p>3 / 52 (5.77%)</p> <p>6</p> <p>2 / 52 (3.85%)</p> <p>2</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Idiopathic pulmonary fibrosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>4 / 52 (7.69%)</p> <p>5</p> <p>3 / 52 (5.77%)</p> <p>5</p> <p>2 / 52 (3.85%)</p> <p>6</p>		
<p>Skin and subcutaneous tissue disorders</p> <p>Alopecia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>10 / 52 (19.23%)</p> <p>10</p> <p>4 / 52 (7.69%)</p> <p>6</p>		
<p>Psychiatric disorders</p> <p>Insomnia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 52 (3.85%)</p> <p>3</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pain in extremity</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>2 / 52 (3.85%)</p> <p>3</p> <p>2 / 52 (3.85%)</p> <p>2</p>		

Infections and infestations Lower respiratory tract infection subjects affected / exposed occurrences (all)	3 / 52 (5.77%) 4		
--	---------------------	--	--

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2021	Protocol version 5.0; Global substantial amendment to protocol version 4.0 included the following changes: 12-week efficacy objective was added. Changes of in-and exclusion criteria: Inclusion criterion 5 modified to include a check at visit 2. Exclusion criterion 1 modified to exclude all types of anti-fibrotic treatment. Exclusion criterion 7 narrowed to only exclude concomitant treatment with strong CYP3A4 inhibitors and inducers, and "or equivalent" added after doses of prednisolone. Exclusion criterion 8 modified to only exclude concomitant treatment with sulphasalazine, rosuvastatin and/or high dose BCRP sensitive substrates.
27 May 2021	Protocol version 6.0; Global Substantial amendment to protocol version 5.0 included the following changes: Anticipated enrollment changed from 60 subjects in total to 60 subjects with a completed week 12 visit. Inclusion criterion 8 added requiring that subjects are fully vaccinated against COVID-19 prior to visit 1. Exclusion criterion 5 moderate to severe hepatic impairment added. Exclusion criterion 9 updated to clarify that only subjects with clinically significant cardiac arrhythmias should be excluded. Criterion 9 further updated to exclude subjects with increased AST, AST or bilirubin values. 5.5.2 Withdrawal from Trial Replacement subjects added for subjects withdrawing prior to week 12 until 60 subjects have completed week 12. 6.2 Number of Subjects Anticipated enrollment changed from 60 subjects in total to 60 subjects with a completed week 12 visit. 6.5.1 Screening (Visit 1) Check of COVID-19 vaccination status added to visit 1 procedure. 9.3 Reporting of Adverse Events For AEs concerning hair loss, additional data collection added.
15 September 2021	Protocol version 7.0; Global Substantial amendment to protocol version 6.0 included the following changes: Inclusion criterion 1 modified from a diagnosis of IPF within 3 years to a diagnosis of IPF within 5 years prior to visit 1. Inclusion criterion 4 modified to allow an FVC of >60 % predicted in UK subjects who have discontinued antifibrotic treatment or refused such treatments. Exclusion criterion 1 updated to allow subjects who have been treated with antifibrotics for ≤6 months. Antifibrotic treatment within 4 weeks prior to visit 1 added to exclusion criterion 7 and disallowed medication Exclusion criterion 18 added to exclude subjects discontinuing or changing antifibrotic treatment due to disease progression.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported