Clinical trial results:
A subject-, investigator-, and sponsor-blinded, randomized, placebo-controlled, multicenter study to investigate efficacy, safety, and tolerability of VAY736 in patients with idiopathic pulmonary fibrosis

Summary

EudraCT number	2017-002667-17
Trial protocol	GB IE DE IT FR
Global end of trial date	14 February 2022

Results information

Result version number	v1 (current)
This version publication date	02 March 2023
First version publication date	02 March 2023

Trial information

Trial identification

Sponsor protocol code	CVAY736X2207

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03287414
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, 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	14 February 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 February 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of VAY736 in patients with IPF by looking at the change from baseline to end-of-treatment (48 weeks of treatment) in forced vital capacity (FVC).

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	20 December 2017
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	Canada: 1
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	30
EEA total number of subjects	17

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	0
Adults (18-64 years)	8
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted across 16 centers in 6 countries.

Pre-assignment

Screening details:

A total of 142 participants were screened of which 30 participants were randomized. 1 participant in the VAY736 arm did not receive treatment as the patient withdrew consent before first dosing.

Period 1

Period 1 title	Treatment Epoch (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	VAY736

Arm description:

Participants received 300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy

Arm type	Experimental
Investigational medicinal product name	Ianalumab
Investigational medicinal product code	VAY736sub
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks

Arm title	Placebo

Arm description:

Participants received placebo administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo administered subcutaneously every 4 weeks for 48 weeks

Number of subjects in period 1[1]	VAY736	Placebo
Started	13	16
Completed	6	12
Not completed	7	4
Study terminated by Sponsor	2	2
Discontinued early with reason "other" selected	1	1
Adverse event, non-fatal	-	1
Subject/Guardian decision	4	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 1 participant randomized was never treated

Baseline characteristics

Reporting groups	
Reporting group title	VAY736
Reporting group description:	
Participants received 300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	

Reporting group values	VAY736	Placebo	Total
Number of subjects	13	16	29
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	5	8
From 65-84 years	10	11	21
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	69.7	68.3	
standard deviation	± 9.30	± 8.15	-
Gender categorical Units: Subjects			
Female	1	1	2
Male	12	15	27
Race/Ethnicity Units: Subjects			
White	13	16	29

End points

End points reporting groups

Reporting group title	VAY736
Reporting group description:	
Participants received 300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	
Reporting group title	Placebo
Reporting group description:	
Participants received placebo administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	

Primary: Change from baseline to end of treatment epoch (48 weeks of treatment) in Forced Vital Capacity (FVC)

End point title	Change from baseline to end of treatment epoch (48 weeks of treatment) in Forced Vital Capacity (FVC)
End point description:	
FVC was defined as the maximum amount of air that an individual was able to forcibly exhale from his / her lungs after taking the deepest breath they could. Change from baseline to end of treatment epoch (48 weeks of treatment) in Forced Vital Capacity (FVC) was analyzed using a Mixed Effects Model for Repeated Measures (MMRM) and considering all assessments collected during the treatment epoch. The model included treatment and visit as fixed effects, standard of care treatment (Nintedanib, Pirfenidone, or no treatment) as factor and baseline value as a covariate, treatment-by-visit and baseline-by-visit as interaction terms. A positive change from baseline indicates improvement. Baseline was defined as the last available assessment pre-dose before or on randomization date.	
End point type	Primary
End point timeframe:	
From baseline up to 48 weeks post first dose of study treatment	

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	16		
Units: Liter (L)				
least squares mean (standard error)	0.039 (± 0.1116)	-0.023 (± 0.0773)		

Statistical analyses

Statistical analysis title	Change from baseline in FVC
Comparison groups	VAY736 v Placebo

Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3248 [1]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.063
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.115
upper limit	0.241
Variability estimate	Standard error of the mean
Dispersion value	0.1379

Notes:

[1] - 1-sided p-values were obtained using MMRM Model.

Secondary: Percentage of participants with all-cause mortality events

End point title	Percentage of participants with all-cause mortality events

End point description:

All-cause mortality events were defined as deaths due to any cause. Kaplan-Meier estimates of the percentage of participants with the event of interest along with 80% two-sided confidence intervals using Greenwood's formula are provided.

End point type	Secondary

End point timeframe:

Up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Percentage of participants				
number (confidence interval 80%)	8.3 (2.39 to 26.92)	0 (-9999 to 9999)		

Statistical analyses

Statistical analysis title	Survival Analysis: All-cause mortality
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.868
Method	Logrank

Secondary: Percentage of participants with survival Idiopathic Pulmonary Fibrosis (IPF) -related mortality events

End point title	Percentage of participants with survival Idiopathic Pulmonary Fibrosis (IPF) -related mortality events

End point description:

IPF-related mortality events were defined as deaths due to IPF related cause. Kaplan-Meier estimates of the percentage of participants with the event of interest along with 80% two-sided confidence intervals using Greenwood's formula are provided.

End point type	Secondary

End point timeframe:

Up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Percentage of participants				
number (confidence interval 80%)	0 (-9999 to 9999)	0 (-9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Progression-free survival (PFS) events

End point title	Percentage of participants with Progression-free survival (PFS) events

End point description:

PFS events were divided into: 1) PFS1 events including progression (relative reduction in FVC ≥ 10%) or death due to all causes, and 2) PFS2 events including progression (relative reduction in FVC ≥ 10%) or death due to IPF-related causes. Kaplan-Meier estimates of the percentage of participants with the event of interest (PFS1 events or PFS2 events) along with 80% two-sided confidence intervals using Greenwood's formula are provided.

End point type	Secondary

End point timeframe:

Up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Percentage of participants				
number (confidence interval 80%)				
PFS1	61.0 (38.22 to 84.20)	31.9 (18.04 to 52.51)		
PFS2	57.1 (33.44 to 82.86)	31.9 (18.04 to 52.51)		

Statistical analyses

Statistical analysis title	Survival analysis: PFS1
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.921
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.6
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.1
upper limit	6.3

Statistical analysis title	Survival analysis: PFS2
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.863
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.9
upper limit	5.6

Secondary: Percentage of participants with disease progression events

End point title	Percentage of participants with disease progression events

End point description:

The following disease progression events were considered: a) relative reduction in FVC ≥ 10%; b) relative reduction in Diffusing Capacity of the Lungs (DLCO) ≥ 15%; c) absolute reduction in Six Minute Walk Distance (6MWD) ≥ 50 m. Kaplan-Meier estimates of the percentage of participants with the event of interest along with 80% two-sided confidence intervals using Greenwood's formula are provided.

End point type	Secondary

End point timeframe:

Up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Percentage of participants				
number (confidence interval 80%)				
FVC	57.1 (33.44 to 82.86)	31.9 (18.08 to 52.51)		
DLCO	73.8 (46.56 to 92.24)	56.1 (36.65 to 75.10)		
6MWD	38.3 (19.96 to 64.88)	75.0 (58.52 to 88.74)		

Statistical analyses

Statistical analysis title	Survival Analysis: FVC
Comparison groups	Placebo v VAY736
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.863
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.2
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.9
upper limit	5.6

Statistical analysis title	Survival Analysis: DLCO
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.457
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9

Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.4
upper limit	2

Statistical analysis title	Survival Analysis: 6MWD
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.019
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.3
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.1
upper limit	0.6

Secondary: Percentage of participants with composite events

End point title	Percentage of participants with composite events

End point description:

Composite events were defined as: 1) death (all-cause mortality), or relative reduction in FVC ≥ 10%, or relative reduction in DLCO ≥ 15%, or relative reduction in 6MWD ≥ 50 m (composite endpoint 1); and 2) Death (IPF-related mortality), or relative reduction in FVC ≥ 10%, or relative reduction in DLCO ≥ 15%, or relative reduction in 6MWD ≥ 50 m (composite endpoint 2). Kaplan-Meier estimates of the percentage of participants with the event of interest along with 80% two-sided confidence intervals using Greenwood’s formula are provided

End point type	Secondary

End point timeframe:

Up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	16		
Units: Percentage of participants				
number (confidence interval 80%)				
Composite Endpoint 1	81.0 (63.86 to 93.29)	66.3 (50.84 to 81.18)		
Composite Endpoint 2	79.2 (61.07 to 92.70)	66.3 (50.84 to 81.18)		

Statistical analyses

Statistical analysis title	Survival Analysis: Composite Endpoint 1
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.611
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.6
upper limit	2

Statistical analysis title	Survival Analysis: Composite Endpoint 2
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	28
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.549
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.1
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.6
upper limit	1.9

Secondary: Change from baseline to end of treatment epoch (48 weeks of treatment) in Diffusing Capacity of the Lungs

End point title	Change from baseline to end of treatment epoch (48 weeks of treatment) in Diffusing Capacity of the Lungs

End point description:

DLCO is a measurement to assess the lungs' ability to transfer gas from inspired air to the bloodstream. DLCO was determined according to ATS guidelines. Change from baseline to end of treatment epoch (48 weeks of treatment) in diffusing capacity of the lung for carbon monoxide (DLCO) was analyzed using a Mixed Effects Model for Repeated Measures (MMRM) and considering all assessments collected during the treatment epoch. The model included treatment and visit as fixed effects, standard of care

treatment (Nintedanib, Pirfenidone, or no treatment) as factor and baseline value as a covariate, treatment-by-visit and baseline-by-visit as interaction terms. A positive change from baseline indicates improvement.
Baseline was defined as the last available assessment pre-dose before or on randomization date.

End point type	Secondary

End point timeframe:

From baseline up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	7		
Units: mililiter/minute/millimeter Mercury				
least squares mean (standard error)	-1.954 (± 1.0816)	-1.033 (± 0.7244)		

Statistical analyses

Statistical analysis title	Change from baseline in DLCO
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.7576 [2]
Method	MMRM
Parameter estimate	Least Squares of the Mean
Point estimate	-0.92
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-2.615
upper limit	0.774
Variability estimate	Standard error of the mean
Dispersion value	1.3109

Notes:

[2] - 1-sided p-values were obtained using MMRM Model.

Secondary: Change from baseline to the end of treatment epoch (48 weeks of treatment) in 6-minute walk distance (6MWD)

End point title	Change from baseline to the end of treatment epoch (48 weeks of treatment) in 6-minute walk distance (6MWD)

End point description:

A standardized 6-minute walk test (6MWT) was performed in accordance with the guidelines of the American Thoracic Society 2002. The distance walked in six minutes (6MWD) was recorded. Change from baseline to end of treatment epoch (48 weeks of treatment) in 6MWD was analyzed using a Mixed Effects Model for Repeated Measures (MMRM) and considering all assessments collected during the treatment epoch. The model included treatment and visit as fixed effects, standard of care treatment (Nintedanib, Pirfenidone, or no treatment) as factor and baseline value as a covariate, treatment-by-visit and baseline-by-visit as interaction terms. A positive change from baseline indicates improvement.

Baseline was defined as the last available assessment pre-dose before or on randomization date.

End point type	Secondary

End point timeframe:

From baseline up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	7		
Units: Meter (m)				
least squares mean (standard error)	19.743 (± 19.743)	-12.479 (± 28.9400)		

Statistical analyses

Statistical analysis title	Change from baseline in 6MWD
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3018 [3]
Method	MMRM
Parameter estimate	Least Squares of the Mean
Point estimate	32.222
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-47.572
upper limit	112.015
Variability estimate	Standard error of the mean
Dispersion value	61.8632

Notes:

[3] - Change from baseline in 6MWD

Secondary: Change from baseline to the end of treatment epoch (48 weeks of treatment) in distance saturation product

End point title	Change from baseline to the end of treatment epoch (48 weeks of treatment) in distance saturation product

End point description:

Distance saturation product is the product of distance walked and lowest oxygen saturation during the 6-min walk test. Change from baseline to end of treatment epoch (48 weeks of treatment) in distance saturation product was analyzed using a Mixed Effects Model for Repeated Measures (MMRM) and considering all assessments collected during the treatment epoch. The model included treatment and visit as fixed effects, standard of care treatment (Nintedanib, Pirfenidone, or no treatment) as factor and baseline value as a covariate, treatment-by-visit and baseline-by-visit as interaction terms. A positive change from baseline indicates improvement. Baseline was defined as the last available assessment pre-dose before or on randomization date.

End point type	Secondary

End point timeframe:

From baseline up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	7		
Units: Meter% (m%)				
least squares mean (standard error)	9.746 (± 52.2985)	-19.420 (± 28.3755)		

Statistical analyses

Statistical analysis title	Distance saturation product
Comparison groups	VAY736 v Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.314 [4]
Method	MMRM
Parameter estimate	Least Squares of the Mean
Point estimate	29.166
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-48.22
upper limit	106.553
Variability estimate	Standard error of the mean
Dispersion value	60.0143

Notes:

[4] - 1-sided p-values were obtained using MMRM Model.

Secondary: Change from baseline to the end of treatment epoch (48 weeks of treatment) in resting oxygen saturation level (on room air)

End point title	Change from baseline to the end of treatment epoch (48 weeks of treatment) in resting oxygen saturation level (on room air)

End point description:

Change from baseline to end of treatment epoch (48 weeks of treatment) in resting oxygen saturation (on room air) was analyzed using a Mixed Effects Model for Repeated Measures (MMRM) and considering all assessments collected during the treatment epoch. The model included treatment and visit as fixed effects, standard of care treatment (Nintedanib, Pirfenidone, or no treatment) as factor and baseline value as a covariate, treatment-by-visit and baseline-by-visit as interaction terms. A positive change from baseline indicates improvement. Baseline was defined as the last available assessment pre-dose before or on randomization date.

End point type	Secondary

End point timeframe:

From baseline up to 48 weeks post first dose of study treatment

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: Percentage (%)				
least squares mean (standard error)	-0.117 (± 1.0179)	-1.887 (± 0.9415)		

Statistical analyses

Statistical analysis title	Resting oxygen saturation level
Comparison groups	Placebo v VAY736
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1269 [5]
Method	MMRM
Parameter estimate	Least Squares of the mean
Point estimate	1.77
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	-0.219
upper limit	3.759
Variability estimate	Standard error of the mean
Dispersion value	1.5422

Notes:

[5] - 1-sided p-values were obtained using MMRM Model.

Secondary: Number of participants with positive serum anti-VAY736 antibodies

End point title	Number of participants with positive serum anti-VAY736 antibodies

End point description:

Number of participants with positive serum anti-VAY736 antibodies. A bridging ELISA method that is designed to detect the presence of anti-VAY736 antibodies in human serum was used.

End point type	Secondary

End point timeframe:

Day 1, 29, 85, 169, 253 and 337

End point values	VAY736	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	15		
Units: Participants				
Day 1	1	3		
Day 29	1	2		
Day 85	1	1		
Day 169	0	2		
Day 253	2	1		
Day 337	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Ctrough of VAY736 from the serum concentration-time data

End point title	Ctrough of VAY736 from the serum concentration-time data[6]

End point description:

At pre-dose on Day 1, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309 and 337

End point type	Secondary

End point timeframe:

At pre-dose on Day 1, 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309 and 337

Notes:

[6] - 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: This endpoint is only applicable for VAY736 arm

End point values	VAY736			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: nanogram (ng) / mililiter (mL)				
arithmetic mean (standard deviation)				
Day 1	0.00 (± 0.00)			
Day 29	676.79 (± 499.931)			
Day 57	779.89 (± 645.363)			
Day 85	786.63 (± 501.225)			
Day 113	771.88 (± 623.268)			
Day 141	1316.05 (± 877.240)			
Day 169	1019.00 (± 587.097)			
Day 197	985.50 (± 495.652)			
Day 225	1271.10 (± 863.055)			
Day 253	998.57 (± 947.343)			

Day 281	705.00 (± 997.021)			
Day 309	827.40 (± 678.836)			
Day 337	688.50 (± 1172.12)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start up to end of study, assessed up to approximately 2.4 years	
Adverse event reporting additional description:	
Safety analyses were performed in the safety set including all participants who received at least one dose of any study drug	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	VAY736
Reporting group description:	
Participants received 300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	
Reporting group title	Placebo
Reporting group description:	
Participants received 300 mg VAY736 administered subcutaneously every 4 weeks for 48 weeks on top of current standard-of-care therapy	
Reporting group title	Total
Reporting group description:	
Total	

Serious adverse events	VAY736	Placebo	Total
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 13 (38.46%)	9 / 16 (56.25%)	14 / 29 (48.28%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Vasculitis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal vein occlusion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic pulmonary fibrosis			

subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	3 / 16 (18.75%)	3 / 29 (10.34%)
occurrences causally related to treatment / all	0 / 0	1 / 3	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	VAY736	Placebo	Total
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	15 / 16 (93.75%)	28 / 29 (96.55%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Keratoacanthoma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Dysplastic naevus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Basal cell carcinoma			

subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	2
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Hypertension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Chest discomfort			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	2 / 13 (15.38%)	1 / 16 (6.25%)	3 / 29 (10.34%)
occurrences (all)	2	2	4
Injection site bruising			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Injection site dermatitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	2	0	2
Injection site erythema			
subjects affected / exposed	2 / 13 (15.38%)	1 / 16 (6.25%)	3 / 29 (10.34%)
occurrences (all)	2	1	3
Injection site inflammation			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Injection site pain			

subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Injection site warmth			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Injection site rash			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Injection site pruritus			
subjects affected / exposed	3 / 13 (23.08%)	2 / 16 (12.50%)	5 / 29 (17.24%)
occurrences (all)	8	2	10
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Dysphonia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	3 / 13 (23.08%)	1 / 16 (6.25%)	4 / 29 (13.79%)
occurrences (all)	3	1	4
Epistaxis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Idiopathic pulmonary fibrosis			
subjects affected / exposed	1 / 13 (7.69%)	3 / 16 (18.75%)	4 / 29 (13.79%)
occurrences (all)	1	3	4
Hypoxia			

subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Insomnia			
subjects affected / exposed	2 / 13 (15.38%)	1 / 16 (6.25%)	3 / 29 (10.34%)
occurrences (all)	2	1	3
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Antinuclear antibody increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Blood creatinine increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood creatine phosphokinase decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood glucose increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood parathyroid hormone decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood potassium increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood triglycerides increased			

subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Blood urea increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Blood urine present			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Escherichia test positive			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Glucose urine present			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Lymphocyte count decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Hepatic enzyme increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Mean cell volume increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Monocyte count increased			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Neutrophil count increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Protein urine present			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1

Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
White blood cell count increased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	4 / 16 (25.00%)	5 / 29 (17.24%)
occurrences (all)	1	4	5
Urine analysis abnormal			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Urine protein/creatinine ratio increased			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	1	1	2
Facial bones fracture			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Heat stroke			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Injection related reaction			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	4	0	4
Sunburn			
subjects affected / exposed	0 / 13 (0.00%)	2 / 16 (12.50%)	2 / 29 (6.90%)
occurrences (all)	0	2	2
Cardiac disorders			
Aortic valve incompetence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1

Arteriosclerosis coronary artery			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Palpitations			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Tachycardia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Cervical radiculopathy			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 13 (15.38%)	2 / 16 (12.50%)	4 / 29 (13.79%)
occurrences (all)	3	2	5
Carotid artery stenosis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Paraesthesia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Memory impairment			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Tremor			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Blood and lymphatic system disorders			

Eosinophilia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Eustachian tube dysfunction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Tinnitus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Eye disorders			
Cataract			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Corneal degeneration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Ocular hyperaemia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Diarrhoea			
subjects affected / exposed	3 / 13 (23.08%)	1 / 16 (6.25%)	4 / 29 (13.79%)
occurrences (all)	3	1	4
Dyspepsia			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Enteritis			

subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Flatulence			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Frequent bowel movements			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Nausea			
subjects affected / exposed	1 / 13 (7.69%)	2 / 16 (12.50%)	3 / 29 (10.34%)
occurrences (all)	1	3	4
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	2 / 16 (12.50%)	3 / 29 (10.34%)
occurrences (all)	1	2	3
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Dermatitis atopic			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Drug eruption			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Hyperhidrosis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Keloid scar			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Pruritus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	2	2

Rash erythematous			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Rash			
subjects affected / exposed	0 / 13 (0.00%)	2 / 16 (12.50%)	2 / 29 (6.90%)
occurrences (all)	0	3	3
Skin lesion			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Pollakiuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Haematuria			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Urinary incontinence			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Limb discomfort			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Muscle spasms			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Osteoporosis			

subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Musculoskeletal pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Pain in extremity			
subjects affected / exposed	2 / 13 (15.38%)	0 / 16 (0.00%)	2 / 29 (6.90%)
occurrences (all)	2	0	2
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 13 (15.38%)	2 / 16 (12.50%)	4 / 29 (13.79%)
occurrences (all)	2	3	5
Conjunctivitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	1 / 16 (6.25%)	3 / 29 (10.34%)
occurrences (all)	2	1	3
Lower respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 16 (6.25%)	2 / 29 (6.90%)
occurrences (all)	2	1	3
Influenza			
subjects affected / exposed	1 / 13 (7.69%)	0 / 16 (0.00%)	1 / 29 (3.45%)
occurrences (all)	1	0	1
Rhinitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Tooth infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	1	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 13 (15.38%)	2 / 16 (12.50%)	4 / 29 (13.79%)
occurrences (all)	5	2	7
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 16 (6.25%)	1 / 29 (3.45%)
occurrences (all)	0	2	2

Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 16 (6.25%) 1	2 / 29 (6.90%) 2
Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 16 (0.00%) 0	1 / 29 (3.45%) 1
Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 16 (0.00%) 0	1 / 29 (3.45%) 1
Decreased appetite subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 16 (6.25%) 1	1 / 29 (3.45%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 August 2017	This amendment corrected an inconsistency within the protocol around the potential need to follow-up partners of patients who could become pregnant during the study. At the time of this amendment, there were no patients enrolled
23 October 2017	This amendment clarified that the St. George's Respiratory Questionnaire in IPF (SGRQ-I) was not available for use in all study countries planned in this study.
08 December 2017	This amendment addressed questions from MHRA upon their initial review of the study protocol.
27 February 2018	This amendment addressed questions from the Irish and French Health Authorities upon their initial reviews of the study protocol. In addition, the baseline visit was removed in order to reduce patient burden, as similar assessments were scheduled to be captured during Treatment Epoch Day 1
03 December 2018	This amendment corrected an error in the definition of a serious adverse event (SAE). The bullet formatting was corrected, and missing text was added to clarify when inpatient hospitalization or prolongation of an existing hospitalization was considered a SAE.
10 July 2019	The purpose of this amendment was to: (a) adjust the sample size and timing of the IA to align with clinical development strategy (b) reduce protocol complexity and (c) implement other minor updates throughout the protocol for clarity.
27 March 2020	This amendment revised the eligibility criteria with the aim of accelerating enrollment

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, data using 9999 as data points in this record are not an accurate representation of the results. Moreover, disposition in PK and PD/safety Follow-up Epochs could not be added. Please use https://www.novctrd.com

Notes: