Clinical trial results:
A Phase IIb, Randomized (Stratified), Double-Blind (Sponsor Open), Parallel-Group, Placebo-Controlled, Dose-Finding Study of Nemiralisib (GSK2269557) Added to Standard of Care (SoC) Versus SoC Alone in Participants Diagnosed with an Acute Moderate or Severe Exacerbation of Chronic Obstructive Pulmonary Disease (COPD)

Summary

EudraCT number	2017-001074-42
Trial protocol	NL SE GB PL DE ES IT
Global end of trial date	10 January 2019

Results information

Result version number	v2 (current)
This version publication date	01 February 2020
First version publication date	18 December 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	200879

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 8664357343, GSKClinicalSupportHD@gsk.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	30 April 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	10 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To characterize the dose response of nemiralisib administered in addition to SoC compared with placebo and SoC in participants diagnosed with an acute moderate or severe exacerbation of COPD

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 November 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Argentina: 103
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 84
Country: Number of subjects enrolled	Italy: 43
Country: Number of subjects enrolled	Korea, Republic of: 68
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	Netherlands: 27
Country: Number of subjects enrolled	Poland: 89
Country: Number of subjects enrolled	Romania: 88
Country: Number of subjects enrolled	Russian Federation: 101
Country: Number of subjects enrolled	Spain: 114
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	United States: 126
Worldwide total number of subjects	943
EEA total number of subjects	484

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)	430
From 65 to 84 years	513
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a Phase IIb, multicenter, randomized, stratified, double-blind (sponsor open), placebo controlled parallel-group study in participants who presented with an acute moderate or severe exacerbation of chronic obstructive pulmonary disease (COPD) requiring Standard of Care (SoC).

Pre-assignment

Screening details:

A total of 943 participants were randomized, and 938 participants who received at least one dose of study treatment were included in the modified intent to treat (MITT) Population. The study included participants enrolled from 16 countries.

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, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants were administered a single oral inhalation of placebo via ELLIPTA dry powder inhaler (DPI) once daily in the morning for 12 weeks. Albuterol (salbutamol) metered-dose inhaler (MDI) or nebules were also provided to all participants as rescue medication.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received placebo as dry powder inhalation once in the morning.

Arm title	Nemiralisib 12.5 mcg

Arm description:

Participants were administered a single oral inhalation of 12.5 micrograms (mcg) nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration of 12.5 micrograms (mcg) as dry powder inhalation once in the morning.

Arm title	Nemiralisib 50 mcg

Arm description:

Participants were administered a single oral inhalation of 50 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all

participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration of 50 mcg as dry powder inhalation once in the morning.

Arm title	Nemiralisib 100 mcg

Arm description:

Participants were administered a single oral inhalation of 100 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration of 100 mcg as dry powder inhalation once in the morning.

Arm title	Nemiralisib 250 mcg

Arm description:

Participants were administered a single oral inhalation of 250 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration 250 mcg as dry powder inhalation once in the morning.

Arm title	Nemiralisib 500 mcg

Arm description:

Participants were administered a single oral inhalation of 500 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration of 500 mcg as dry powder inhalation once in the morning.

Arm title	Nemiralisib 750 mcg

Arm description:

Participants were administered a single oral inhalation of 750 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Arm type	Active comparator
Investigational medicinal product name	Nemiralisib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received Nemiralisib at concentration of 750 mcg as dry powder inhalation once in the morning.

Number of subjects in period 1[1]	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg
Started	276	22	91
Completed	244	19	79
Not completed	32	3	12
Protocol deviation	2	-	-
Physician decision	3	1	-
Lack of efficacy	1	1	1
Adverse event, non-fatal	4	-	5
Consent withdrawn by subject	11	1	5
Protocol-defined stopping criteria	9	-	-
Lost to follow-up	2	-	1

Number of subjects in period 1[1]	Nemiralisib 100 mcg	Nemiralisib 250 mcg	Nemiralisib 500 mcg
Started	92	90	89
Completed	81	75	73
Not completed	11	15	16
Protocol deviation	-	1	-
Physician decision	-	1	2
Lack of efficacy	1	1	-
Adverse event, non-fatal	4	6	5
Consent withdrawn by subject	6	3	6
Protocol-defined stopping criteria	-	2	1
Lost to follow-up	-	1	2

Number of subjects in period 1[1]	Nemiralisib 750 mcg
Started	278
Completed	233

Not completed	45
Protocol deviation	3
Physician decision	3
Lack of efficacy	3
Adverse event, non-fatal	16
Consent withdrawn by subject	16
Protocol-defined stopping criteria	1
Lost to follow-up	3

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: 943 participants were randomized, and 938 participants who received at least one dose of study treatment were included in the MITT Population.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Participants were administered a single oral inhalation of placebo via ELLIPTA dry powder inhaler (DPI) once daily in the morning for 12 weeks. Albuterol (salbutamol) metered-dose inhaler (MDI) or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 12.5 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 12.5 micrograms (mcg) nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 50 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 50 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 100 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 100 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 250 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 250 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 500 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 500 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 750 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 750 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	

Reporting group values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg
Number of subjects	276	22	91
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)	123	9	44
From 65-84 years	153	13	47

85 years and over	0	0	0

Age Continuous			
Units: Years			
arithmetic mean	65.4	67.8	63.1
standard deviation	± 7.94	± 7.20	± 7.61
Sex: Female, Male			
Units: Subjects			
Female	86	6	35
Male	190	16	56
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian-East Asian Heritage	18	4	7
Asian-South East Asian Heritage	1	0	0
Black or African American	2	1	2
White-Arabic/North African Heritage	1	0	1
White-White Caucasian/European Heritage	252	17	79

Reporting group values	Nemiralisib 100 mcg	Nemiralisib 250 mcg	Nemiralisib 500 mcg
Number of subjects	92	90	89
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)	38	39	41
From 65-84 years	54	51	48
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	65.1	66.0	64.9
standard deviation	± 7.43	± 6.94	± 8.04
Sex: Female, Male			
Units: Subjects			
Female	29	31	22
Male	63	59	67
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	1	2	2
Asian-East Asian Heritage	2	9	7
Asian-South East Asian Heritage	1	0	1
Black or African American	1	0	2
White-Arabic/North African Heritage	1	0	1

White-White Caucasian/European Heritage	86	79	76

Reporting group values	Nemiralisib 750 mcg	Total	
Number of subjects	278	938	
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)	134	428	
From 65-84 years	144	510	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	64.8		
standard deviation	± 7.61	-	
Sex: Female, Male Units: Subjects			
Female	100	309	
Male	178	629	
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	6	15	
Asian-East Asian Heritage	19	66	
Asian-South East Asian Heritage	1	4	
Black or African American	6	14	
White-Arabic/North African Heritage	0	4	
White-White Caucasian/European Heritage	246	835	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Participants were administered a single oral inhalation of placebo via ELLIPTA dry powder inhaler (DPI) once daily in the morning for 12 weeks. Albuterol (salbutamol) metered-dose inhaler (MDI) or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 12.5 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 12.5 micrograms (mcg) nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 50 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 50 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 100 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 100 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 250 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 250 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 500 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 500 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	
Reporting group title	Nemiralisib 750 mcg
Reporting group description:	
Participants were administered a single oral inhalation of 750 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.	

Primary: Change from Baseline in Clinic Visit trough forced expiratory volume in one second (FEV1) at Day 84 measured post bronchodilator

End point title	Change from Baseline in Clinic Visit trough forced expiratory volume in one second (FEV1) at Day 84 measured post bronchodilator
End point description:	
Post-bronchodilator FEV1 was conducted approximately 10-30 minutes after administration of 4 inhalations of albuterol (salbutamol) via MDI using spacer/valved-holding chamber or via 1 nebulized treatment. Post-bronchodilator Baseline FEV1 is latest FEV1 measured prior to first dose of study treatment and post-bronchodilator. Change from Baseline in clinic visit trough FEV1 at Day 84 measured post-bronchodilator is FEV1 measured prior to dosing and post-bronchodilator on Day 84 minus post-bronchodilator Baseline FEV1. Bayesian repeated measure model adjusted for Baseline by visit interaction, treatment by visit interaction, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in previous 12 months and gender was used. Posterior adjusted median change from Baseline and 95% highest posterior density (HPD) credible interval (CrI) was presented. Only those participants with data at specified data points were analyzed.	
End point type	Primary

End point timeframe:

Baseline and Day 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	215[1]	16[2]	72[3]	75[4]
Units: Liters				
median (confidence interval 95%)	0.052 (0.018 to 0.091)	0.031 (-0.090 to 0.149)	0.026 (-0.036 to 0.084)	0.014 (-0.044 to 0.073)

Notes:

[1] - MITT Population consists of randomized participants who received atleast 1 dose of study treatment.

[2] - MITT Population.

[3] - MITT Population.

[4] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69[5]	58[6]	216[7]	
Units: Liters				
median (confidence interval 95%)	0.058 (-0.002 to 0.118)	0.049 (-0.017 to 0.113)	0.049 (0.012 to 0.086)	

Notes:

[5] - MITT Population.

[6] - MITT Population.

[7] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Nemiralisib 12.5 mcg v Placebo
Number of subjects included in analysis	231
Analysis specification	Pre-specified
Analysis type	other[8]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.143
upper limit	0.103

Notes:

[8] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 12.5 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	287
Analysis specification	Pre-specified

Analysis type	other[9]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.027
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.098
upper limit	0.036

Notes:

[9] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 50 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	290
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.102
upper limit	0.028

Notes:

[10] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 100 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.064
upper limit	0.071

Notes:

[11] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 250 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	273
Analysis specification	Pre-specified
Analysis type	other[12]

Parameter estimate	Posterior adjusted median difference
Point estimate	-0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.075
upper limit	0.061

Notes:

[12] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 500 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	other[13]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.051
upper limit	0.042

Notes:

[13] - Treatment comparison (posterior adjusted median difference and 95% HPD CrI) of Nemiralisib 750 mcg and placebo for Day 84 change from Baseline FEV1 measured post-bronchodilator has been presented.

Secondary: Rate of moderate and severe exacerbations over 12-week treatment period

End point title	Rate of moderate and severe exacerbations over 12-week treatment period

End point description:

Moderate COPD exacerbations are defined as worsening symptoms of COPD treated with short-acting bronchodilators (SABDs) plus antibiotics and/or oral/systemic corticosteroids. Severe COPD exacerbations are defined as worsening symptoms of COPD that require hospitalization or visit to the emergency room. Severe exacerbation may also be associated with acute respiratory failure. Rate of exacerbations was analyzed using Bayesian Poisson model adjusting for length of on-treatment follow-up, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender. Posterior median exacerbation rate and 95% HPD CrI has been presented. The participants randomized to Nemiralisib 12.5 mcg were excluded from this analysis due to insufficient participants with data.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[14]	22[15]	91[16]	92[17]
Units: No.of exacerbation per 84 Days				
median (confidence interval 95%)	0.31 (0.25 to 0.39)	99999 (99999 to 99999)	0.29 (0.20 to 0.39)	0.28 (0.20 to 0.38)

Notes:

[14] - MITT Population.

[15] - MITT Population.

[16] - MITT Population.

[17] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[18]	89[19]	278[20]	
Units: No.of exacerbation per 84 Days				
median (confidence interval 95%)	0.32 (0.23 to 0.43)	0.20 (0.13 to 0.29)	0.36 (0.29 to 0.43)	

Notes:

[18] - MITT Population.

[19] - MITT Population.

[20] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	Posterior median exacerbation rate ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.4

Notes:

[21] - Treatment comparison (posterior median exacerbation rate ratio and 95% HPD CrI) of Nemiralisib 50 mcg and placebo for moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	Posterior median exacerbation rate ratio
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57

upper limit	1.35

Notes:

[22] - Treatment comparison (posterior median exacerbation rate ratio and 95% HPD CrI) of Nemiralisib 100 mcg and placebo for moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	Posterior median exacerbation rate ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.5

Notes:

[23] - Treatment comparison (posterior median exacerbation rate ratio and 95% HPD CrI) of Nemiralisib 250 mcg and placebo for moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[24]
Parameter estimate	Posterior median exacerbation rate ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1.02

Notes:

[24] - Treatment comparison (posterior median exacerbation rate ratio and 95% HPD CrI) of Nemiralisib 500 mcg and placebo for moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[25]
Parameter estimate	Posterior median exacerbation rate ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.52

Notes:

[25] - Treatment comparison (posterior median exacerbation rate ratio and 95% HPD CrI) of Nemiralisib 750 mcg and placebo for moderate/severe exacerbations has been presented.

Secondary: Number of participants with Time to next moderate/severe exacerbation following index exacerbation

End point title	Number of participants with Time to next moderate/severe exacerbation following index exacerbation

End point description:

Number of participants with time to next (on-treatment) moderate/severe exacerbation following index exacerbation during the 12-Week Treatment Period was defined as time from the date of randomization until the date of onset of the first moderate/severe exacerbation whilst on study treatment. Participants who did not have an exacerbation whilst on study treatment were censored at the date of their last dose of study treatment. Time to next exacerbation was analyzed using a Bayesian Cox proportional hazards model adjusting for treatment group, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[26]	22[27]	91[28]	92[29]
Units: Participants	72	3	24	25

Notes:

[26] - MITT Population.

[27] - MITT Population.

[28] - MITT Population.

[29] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[30]	89[31]	278[32]	
Units: Participants	26	15	80	

Notes:

[30] - MITT Population.

[31] - MITT Population.

[32] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	Posterior median hazard ratio
Point estimate	0.455
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.054
upper limit	1.103

Notes:

[33] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 12.5 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	Posterior median hazard ratio
Point estimate	0.991
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.5

Notes:

[34] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 50 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[35]
Parameter estimate	Posterior median hazard ratio
Point estimate	0.975
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.581
upper limit	1.467

Notes:

[35] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 100 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[36]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.132
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.682
upper limit	1.709

Notes:

[36] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 250 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 5

Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[37]
Parameter estimate	Posterior median hazard ratio
Point estimate	0.556
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.268
upper limit	0.902

Notes:

[37] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 500 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[38]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.149
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	1.539

Notes:

[38] - Treatment comparison (Hazard Ratio and 95% HPD CrI) of Nemiralisib 750 mcg and placebo for time to next moderate/severe exacerbations has been presented.

Secondary: Change from Baseline in Clinic Visit trough FEV1 measured pre and post-bronchodilator

End point title	Change from Baseline in Clinic Visit trough FEV1 measured pre and post-bronchodilator

End point description:

Pulmonary function was measured by FEV1. Post-bronchodilator FEV1 was conducted approximately 10-30 minutes after participant was administered with 4 inhalations of albuterol via MDI using a spacer/valved-holding chamber or via 1 nebulized treatment. Pre-bronchodilator and post-bronchodilator Baseline FEV1 is latest FEV1 measured prior to first dose of study treatment and pre-bronchodilator and post-bronchodilator, respectively. Change from Baseline in clinic visit trough FEV1 at Days 14, 28, 56 and 84 measured pre-bronchodilator is defined as FEV1 measured prior to dosing and pre-bronchodilator on Days 14, 28, 56 and 84 minus pre-bronchodilator Baseline FEV1. Only those participants with data available at specified data points were analyzed (represented by n= X in category titles). 99999 indicates standard deviation could not be calculated as single participant was analyzed. 88888 indicates number of participants analyzed was zero.

End point type	Secondary

End point timeframe:

Baseline and Days 14, 28, 56 (pre and post bronchodilaor), 84 (pre-bronchodilator) and at hospital discharge (maximum 24 Weeks)

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[39]	22[40]	91[41]	92[42]
Units: Liters				
arithmetic mean (standard deviation)				
Day 14, Pre, n=240, 20, 85, 83, 76, 76, 238	0.008 (± 0.2729)	0.100 (± 0.2511)	-0.021 (± 0.2657)	-0.013 (± 0.2509)
Day 14, Post, n=248, 20, 86, 83, 77, 78, 241	0.034 (± 0.2707)	0.075 (± 0.2425)	0.010 (± 0.2168)	-0.050 (± 0.2477)
Day 28, Pre, n=239, 20, 82, 79, 75, 71, 232	0.017 (± 0.2585)	0.081 (± 0.2661)	-0.034 (± 0.2875)	-0.010 (± 0.2333)
Day 28, Post, n=245, 19, 83, 81, 76, 72, 232	0.036 (± 0.2647)	0.059 (± 0.2575)	0.004 (± 0.2183)	-0.034 (± 0.2401)
Day 56, Pre, n=230, 20, 78, 76, 73, 67, 224	0.005 (± 0.2295)	-0.006 (± 0.2636)	-0.024 (± 0.3210)	0.011 (± 0.2415)
Day 56, Post, n=237, 19, 78, 77, 74, 69, 224	0.020 (± 0.2614)	-0.002 (± 0.2252)	-0.012 (± 0.2524)	0.004 (± 0.2373)
Day 84, Pre, n=210, 17, 71, 73, 66, 58, 212	0.000 (± 0.2566)	0.003 (± 0.2232)	-0.049 (± 0.2549)	0.005 (± 0.2668)
Hospital discharge, Pre, n=23, 2, 8, 8, 7, 3, 22	0.071 (± 0.1586)	0.168 (± 0.2652)	0.108 (± 0.3888)	0.056 (± 0.1782)
Hospital discharge, Post, n=8, 2, 1, 1, 1, 0, 6	0.134 (± 0.1514)	0.153 (± 0.0933)	0.083 (± 99999)	-0.076 (± 99999)

Notes:

[39] - MITT Population.

[40] - MITT Population.

[41] - MITT Population.

[42] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[43]	89[44]	278[45]	
Units: Liters				
arithmetic mean (standard deviation)				
Day 14, Pre, n=240, 20, 85, 83, 76, 76, 238	0.053 (± 0.2958)	0.041 (± 0.2738)	0.023 (± 0.2561)	
Day 14, Post, n=248, 20, 86, 83, 77, 78, 241	0.054 (± 0.2983)	0.073 (± 0.2655)	0.044 (± 0.2216)	
Day 28, Pre, n=239, 20, 82, 79, 75, 71, 232	0.064 (± 0.2592)	0.016 (± 0.2713)	0.020 (± 0.2512)	
Day 28, Post, n=245, 19, 83, 81, 76, 72, 232	0.049 (± 0.2639)	0.027 (± 0.2369)	0.029 (± 0.2307)	
Day 56, Pre, n=230, 20, 78, 76, 73, 67, 224	0.022 (± 0.2522)	-0.004 (± 0.2233)	-0.001 (± 0.2858)	
Day 56, Post, n=237, 19, 78, 77, 74, 69, 224	0.026 (± 0.2556)	-0.011 (± 0.2260)	0.011 (± 0.2470)	
Day 84, Pre, n=210, 17, 71, 73, 66, 58, 212	0.015 (± 0.2739)	0.007 (± 0.2461)	0.010 (± 0.2829)	
Hospital discharge, Pre, n=23, 2, 8, 8, 7, 3, 22	0.052 (± 0.3481)	0.162 (± 0.1426)	0.075 (± 0.1974)	
Hospital discharge, Post, n=8, 2, 1, 1, 1, 0, 6	0.094 (± 99999)	88888 (± 99999)	-0.006 (± 0.1079)	

Notes:

[43] - MITT Population.

[44] - MITT Population.

[45] - MITT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from hospital discharge in Clinic Visit trough FEV1 measured pre and post-bronchodilator

End point title	Change from hospital discharge in Clinic Visit trough FEV1 measured pre and post-bronchodilator

End point description:

FEV1, defined as maximal amount of air exhaled forcefully from lungs in 1 second. Post-bronchodilator FEV1 was conducted approximately 10-30 minutes after administration with 4 inhalations of albuterol via MDI using a spacer/valved-holding chamber or via 1 nebulized treatment. Pre- and post-bronchodilator Baseline FEV1 is defined as latest FEV1 measured prior to first dose of study treatment and pre- and post-bronchodilator, respectively. Change from hospital discharge in clinic visit trough FEV1 at Days 14, 28, 56 and 84 measured pre- and post-bronchodilator is defined as FEV1 measured prior to dosing and pre- and post-bronchodilator on Days 14, 28, 56 and 84 minus pre and post-bronchodilator Baseline FEV1. Only those participants with data at specified data points were analyzed (represented by n= X in category titles). 99999 indicates standard deviation could not be calculated as single participant was analyzed. 88888 indicates number of participants analyzed was 0.

End point type	Secondary

End point timeframe:

Baseline and pre- and post-bronchodilator on Days 14, 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[46]	22[47]	91[48]	92[49]
Units: Liters				
arithmetic mean (standard deviation)				
Day 14, Pre, n=20, 2, 8, 8, 6, 4, 20	0.082 (± 0.2783)	0.355 (± 0.4207)	0.069 (± 0.3012)	-0.049 (± 0.1882)
Day 14, Post, n=5, 2, 1, 1, 1, 0, 5	0.056 (± 0.3372)	0.431 (± 0.5190)	0.119 (± 99999)	0.310 (± 99999)
Day 28, Pre, n=37, 2, 14, 8, 10, 9, 37	0.026 (± 0.2691)	0.261 (± 0.5204)	0.012 (± 0.2910)	-0.085 (± 0.2072)
Day 28, Post, n=22, 2, 8, 1, 4, 4, 22	0.034 (± 0.2779)	0.334 (± 0.5614)	0.130 (± 0.2327)	0.130 (± 99999)
Day 56, Pre, n=37, 2, 14, 8, 9, 10, 36	0.019 (± 0.2282)	0.106 (± 0.6138)	0.019 (± 0.3509)	0.014 (± 0.1938)
Day 56, Post, n=22, 2, 7, 1, 4, 5, 21	-0.014 (± 0.2896)	0.139 (± 0.6838)	0.042 (± 0.3068)	0.098 (± 99999)
Day 84, Pre, n=37, 2, 12, 8, 7, 10, 35	0.007 (± 0.2741)	-0.027 (± 0.4554)	0.121 (± 0.2770)	-0.081 (± 0.1738)
Day 84, Post, n=22, 2, 6, 1, 4, 5, 22	-0.039 (± 0.2610)	0.133 (± 0.5162)	0.037 (± 0.3341)	0.108 (± 99999)

Notes:

[46] - MITT Population.

[47] - MITT Population.

[48] - MITT Population.

[49] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[50]	89[51]	278[52]	
Units: Liters				
arithmetic mean (standard deviation)				
Day 14, Pre, n=20, 2, 8, 8, 6, 4, 20	-0.069 (± 0.4905)	0.173 (± 0.5137)	0.002 (± 0.2343)	
Day 14, Post, n=5, 2, 1, 1, 1, 0, 5	-0.305 (± 99999)	88888 (± 99999)	-0.021 (± 0.1326)	
Day 28, Pre, n=37, 2, 14, 8, 10, 9, 37	0.012 (± 0.4020)	0.030 (± 0.4029)	-0.046 (± 0.2639)	
Day 28, Post, n=22, 2, 8, 1, 4, 4, 22	0.009 (± 0.2006)	0.007 (± 0.3237)	-0.094 (± 0.2293)	
Day 56, Pre, n=37, 2, 14, 8, 9, 10, 36	-0.074 (± 0.3847)	-0.042 (± 0.1840)	-0.054 (± 0.2942)	
Day 56, Post, n=22, 2, 7, 1, 4, 5, 21	-0.056 (± 0.3572)	-0.072 (± 0.1490)	-0.135 (± 0.2410)	
Day 84, Pre, n=37, 2, 12, 8, 7, 10, 35	-0.072 (± 0.4391)	0.043 (± 0.2511)	-0.062 (± 0.2816)	
Day 84, Post, n=22, 2, 6, 1, 4, 5, 22	0.021 (± 0.3151)	0.006 (± 0.2180)	-0.106 (± 0.2956)	

Notes:

[50] - MITT Population.

[51] - MITT Population.

[52] - MITT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants achieving the exacerbations of chronic pulmonary disease tool (EXACT) definition of recovery from the index exacerbation

End point title	Percentage of participants achieving the exacerbations of chronic pulmonary disease tool (EXACT) definition of recovery from the index exacerbation

End point description:

EXACT patient-reported outcome (EXACT-PRO), 14-item instrument to capture occurrence, frequency, severity, and duration of exacerbations using an electronic diary (eDiary). Total score ranges from 0-100, higher score indicates more severe condition. Participants were required to complete EXACT-PRO every evening; however, on the day of randomization it was to be completed in the morning. Response was decrease in rolling average EXACT Total Score >=9 points from maximum observed value, sustained for >=7 days, with first of 7 days defined as recovery day. Analysis was performed using Bayesian Cox proportional hazards model adjusting for treatment group, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in previous 12 months and gender.

End point type	Secondary

End point timeframe:

Days 14, 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[53]	22[54]	91[55]	92[56]
Units: Percentage of participants				
Day 14	29	27	37	29
Day 28	40	41	52	43
Day 56	49	45	59	52
Day 84	51	50	59	54

Notes:

[53] - MITT Population.

[54] - MITT Population.

[55] - MITT Population.

[56] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[57]	89[58]	278[59]	
Units: Percentage of participants				
Day 14	28	24	32	
Day 28	42	27	42	
Day 56	50	31	50	
Day 84	50	37	54	

Notes:

[57] - MITT Population.

[58] - MITT Population.

[59] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[60]
Parameter estimate	Posterior median odds ratio
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	2.3

Notes:

[60] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[61]

Parameter estimate	Posterior median odds ratio
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	2.17

Notes:

[61] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[62]
Parameter estimate	Posterior median odds ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.61

Notes:

[62] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[63]
Parameter estimate	Posterior median odds ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.49

Notes:

[63] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[64]
Parameter estimate	Posterior median odds ratio
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.38
upper limit	1.25

Notes:

[64] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[65]
Parameter estimate	Posterior median odds ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.63

Notes:

[65] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 14 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[66]
Parameter estimate	Posterior median odds ratio
Point estimate	1.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	2.69

Notes:

[66] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[67]
Parameter estimate	Posterior median odds ratio
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	2.33

Notes:

[67] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[68]
Parameter estimate	Posterior median odds ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.79

Notes:

[68] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 10
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[69]
Parameter estimate	Posterior median odds ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.74

Notes:

[69] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[70]
Parameter estimate	Posterior median odds ratio
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.28
upper limit	0.88

Notes:

[70] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 12

Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[71]
Parameter estimate	Posterior median odds ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	1.49

Notes:

[71] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[72]
Parameter estimate	Posterior median odds ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	2.17

Notes:

[72] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[73]
Parameter estimate	Posterior median odds ratio
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	2.27

Notes:

[73] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 15
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[74]

Parameter estimate	Posterior median odds ratio
Point estimate	1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.78

Notes:

[74] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[75]
Parameter estimate	Posterior median odds ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.67

Notes:

[75] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 17
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[76]
Parameter estimate	Posterior median odds ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	0.77

Notes:

[76] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 18
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[77]
Parameter estimate	Posterior median odds ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.71
upper limit	1.42

Notes:

[77] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 19
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[78]
Parameter estimate	Posterior median odds ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	2.38

Notes:

[78] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 20
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[79]
Parameter estimate	Posterior median odds ratio
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2

Notes:

[79] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 21
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[80]
Parameter estimate	Posterior median odds ratio
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.71

Notes:

[80] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 22
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[81]
Parameter estimate	Posterior median odds ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.48

Notes:

[81] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 23
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[82]
Parameter estimate	Posterior median odds ratio
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.31
upper limit	0.87

Notes:

[82] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 24
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[83]
Parameter estimate	Posterior median odds ratio
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.47

Notes:

[83] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Secondary: Number of participants with Time to recovery from index exacerbation

using EXACT- PRO tool	
End point title	Number of participants with Time to recovery from index exacerbation using EXACT- PRO tool

End point description:

Time to EXACT-defined recovery from index exacerbation is defined as time from the date of randomization until date of the first EXACT-defined recovery day during the 12-Week Treatment Period. EXACT-defined recovery from the index exacerbation is defined as a decrease in the Rolling Average EXACT total Score >=9 points from the Maximum Observed Value, sustained for >=7 days, with the first of the 7 days defined as the recovery day. Analysis was performed using a Bayesian Cox proportional hazards model adjusting for treatment group, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender. Number of participants reporting events is presented.

End point type	Secondary

End point timeframe:

From randomization to Week 12

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[84]	22[85]	91[86]	92[87]
Units: Participants	141	11	54	50

Notes:

[84] - MITT Population.

[85] - MITT Population.

[86] - MITT Population.

[87] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[88]	89[89]	278[90]	
Units: Participants	45	34	149	

Notes:

[88] - MITT Population.

[89] - MITT Population.

[90] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[91]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.053
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.477
upper limit	1.765

Notes:

[91] - Treatment comparison between placebo and Nemiralisib 12.5 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[92]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.597

Notes:

[92] - Treatment comparison between placebo and Nemiralisib 50 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[93]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.734
upper limit	1.432

Notes:

[93] - Treatment comparison between placebo and Nemiralisib 100 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[94]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.719
upper limit	1.413

Notes:

[94] - Treatment comparison between placebo and Nemiralisib 250 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5

Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[95]
Parameter estimate	Posterior median hazard ratio
Point estimate	0.751
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.487
upper limit	1.057

Notes:

[95] - Treatment comparison between placebo and Nemiralisib 500 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[96]
Parameter estimate	Posterior median hazard ratio
Point estimate	1.149
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.899
upper limit	1.426

Notes:

[96] - Treatment comparison between placebo and Nemiralisib 750 mcg was performed and posterior median hazard ratio and 95% HPD CrI has been presented.

Secondary: Mean severity of subsequent health care resource use (HCRU) exacerbations defined by EXACT

End point title	Mean severity of subsequent health care resource use (HCRU) exacerbations defined by EXACT

End point description:

Severity of subsequent HCRU-defined exacerbations defined by EXACT was defined as the highest EXACT Total Score (not using the 3-day Rolling Average) during the period from date of onset of the subsequent HCRU-exacerbation until date of EXACT-defined recovery of subsequent exacerbation. EXACT-PRO, 14-item instrument to capture occurrence, frequency, severity, and duration of exacerbations using an eDiary. Total score ranges from 0-100, higher score indicates more severe condition. For participants with more than one subsequent exacerbation, severity was calculated for each subsequent exacerbation. Only those participants with data available at specified data points were analyzed (represented by n=X in the category title). 99999 indicates standard deviation could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Up to Week 12

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66[97]	3[98]	23[99]	25[100]
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Moderate/Severe, n=66, 3, 23, 25, 26, 15, 78	53.3 (± 12.16)	64.6 (± 25.20)	59.8 (± 12.82)	50.5 (± 10.76)
Moderate, n=55, 3, 15, 23, 17, 10, 63	53.1 (± 11.54)	60.0 (± 26.56)	57.4 (± 11.08)	50.0 (± 11.15)
Severe, n=13, 1, 9, 3, 10, 6, 20	54.0 (± 15.53)	83.0 (± 99999)	64.0 (± 15.01)	55.3 (± 5.69)

Notes:

[97] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

[98] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

[99] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

[100] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26[101]	15[102]	78[103]	
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Moderate/Severe, n=66, 3, 23, 25, 26, 15, 78	47.5 (± 13.95)	57.6 (± 10.30)	51.9 (± 10.78)	
Moderate, n=55, 3, 15, 23, 17, 10, 63	46.3 (± 14.20)	53.8 (± 9.28)	50.0 (± 10.17)	
Severe, n=13, 1, 9, 3, 10, 6, 20	49.5 (± 13.95)	64.1 (± 8.99)	58.8 (± 10.34)	

Notes:

[101] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

[102] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

[103] - Severity was derived for participants from MITT Population who had reported subsequent exacerbation.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of responders using the COPD Assessment Test (CAT) on treatment Days 28, 56, and 84, and following EXACT defined recovery from the index exacerbation

End point title	Percentage of responders using the COPD Assessment Test (CAT) on treatment Days 28, 56, and 84, and following EXACT defined recovery from the index exacerbation

End point description:

The CAT is a short, self-completed, 8-item questionnaire, each item was rated on a 6-point scale ranging from 0 (no impairment) to 5 (maximum impairment). The total CAT score is calculated by summing the scores of all items and ranges from 0 to 40, higher scores indicating severe condition. The percentage of responders using the CAT is defined as number of participants with a decrease from Baseline in CAT Total Score >=2 on or before Days 28, 56 and 84 divided by total number of participants in the MITT population. Percentage of responders using CAT was derived only for participants with a Baseline CAT Total Score >=2. Analysis was performed using a separate Bayesian logistic regression for each time point adjusting for treatment group, smoking status at baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender.

End point type	Secondary

End point timeframe:
Days 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[104]	22[105]	91[106]	92[107]
Units: Percentage of responders				
Day 28	32	36	34	39
Day 56	63	50	73	61
Day 84	70	55	78	65

Notes:
[104] - MITT Population.
[105] - MITT Population.
[106] - MITT Population.
[107] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[108]	89[109]	278[110]	
Units: Percentage of responders				
Day 28	38	34	25	
Day 56	69	55	61	
Day 84	72	60	66	

Notes:
[108] - MITT Population.
[109] - MITT Population.
[110] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[111]
Parameter estimate	Posterior median odds ratio
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	2.7

Notes:
[111] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[112]
Parameter estimate	Posterior median odds ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.77

Notes:

[112] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[113]
Parameter estimate	Posterior median odds ratio
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	2.17

Notes:

[113] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[114]
Parameter estimate	Posterior median odds ratio
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	2

Notes:

[114] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[115]

Parameter estimate	Posterior median odds ratio
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.75

Notes:

[115] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Anallysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[116]
Parameter estimate	Posterior median odds ratio
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.99

Notes:

[116] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 28 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[117]
Parameter estimate	Posterior median odds ratio
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.41

Notes:

[117] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[118]
Parameter estimate	Posterior median odds ratio
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.84
upper limit	2.46

Notes:

[118] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[119]
Parameter estimate	Posterior median odds ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.48

Notes:

[119] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 10
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[120]
Parameter estimate	Posterior median odds ratio
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	2.16

Notes:

[120] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[121]
Parameter estimate	Posterior median odds ratio
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	1.17

Notes:

[121] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 12
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[122]
Parameter estimate	Posterior median odds ratio
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	1.27

Notes:

[122] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 56 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[123]
Parameter estimate	Posterior median odds ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.2

Notes:

[123] - Treatment comparison between placebo and nemiralisib 12.5 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[124]
Parameter estimate	Posterior median odds ratio
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	2.56

Notes:

[124] - Treatment comparison between placebo and nemiralisib 50 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 15

Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[125]
Parameter estimate	Posterior median odds ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.3

Notes:

[125] - Treatment comparison between placebo and nemiralisib 100 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[126]
Parameter estimate	Posterior median odds ratio
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.86

Notes:

[126] - Treatment comparison between placebo and nemiralisib 250 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 17
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[127]
Parameter estimate	Posterior median odds ratio
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	1.02

Notes:

[127] - Treatment comparison between placebo and nemiralisib 500 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented

Statistical analysis title	Statistical Analysis 18
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[128]

Parameter estimate	Posterior median odds ratio
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.17

Notes:

[128] - Treatment comparison between placebo and nemiralisib 750 mcg at Day 84 was performed and posterior median odds ratio and 95% HPD CrI has been presented.

Secondary: Change from Baseline in CAT total score

End point title	Change from Baseline in CAT total score

End point description:

CAT is a short, self-completed, 8-item questionnaire, each item was rated on a 6-point scale ranging from 0 (no impairment) to 5 (maximum impairment). Total CAT score was calculated by summing scores of all items and ranges from 0 to 40, higher scores indicating more severe condition. Baseline (Day 1) is latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline in CAT Total Score is CAT Total Score on Days 28, 56 and 84 minus Baseline CAT Total Score. Analysis was using Bayesian repeated measures model adjusting for Baseline by visit interaction, treatment by visit interaction, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender. Posterior adjusted median change from Baseline and 95% HPD CrI has been presented. Only those participants with data available at specified data points were analyzed (represented by n= X in category titles).

End point type	Secondary

End point timeframe:

Baseline and at Days 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[129]	22[130]	91[131]	92[132]
Units: Scores on a scale				
median (confidence interval 95%)				
Day 28, n=234, 19, 86, 80, 77, 74, 229	-4.7 (-5.6 to -3.8)	-2.3 (-5.1 to 0.5)	-4.0 (-5.4 to -2.7)	-3.9 (-5.4 to -2.4)
Day 56, n=231, 20, 78, 77, 76, 69, 222	-4.2 (-5.2 to -3.3)	-1.9 (-4.7 to 1.0)	-3.4 (-5.0 to -1.9)	-4.5 (-6.0 to -2.9)
Day 84, n=218, 17, 75, 75, 69, 62, 213	-4.6 (-5.6 to -3.6)	-2.7 (-6.0 to 0.3)	-3.5 (-5.0 to -1.9)	-5.1 (-6.7 to -3.5)

Notes:

[129] - MITT Population.

[130] - MITT Population.

[131] - MITT Population.

[132] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[133]	89[134]	278[135]	
Units: Scores on a scale				
median (confidence interval 95%)				

Day 28, n=234, 19, 86, 80, 77, 74, 229	-5.1 (-6.5 to -3.7)	-3.1 (-4.5 to -1.6)	-4.7 (-5.6 to -3.8)	
Day 56, n=231, 20, 78, 77, 76, 69, 222	-4.8 (-6.4 to -3.4)	-3.8 (-5.5 to -2.3)	-4.4 (-5.4 to -3.5)	
Day 84, n=218, 17, 75, 75, 69, 62, 213	-4.7 (-6.3 to -3.1)	-3.8 (-5.4 to -2.1)	-4.2 (-5.2 to -3.2)	

Notes:

[133] - MITT Population.

[134] - MITT Population.

[135] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[136]
Parameter estimate	Posterior adjusted median difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	5.2

Notes:

[136] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[137]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	2.3

Notes:

[137] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[138]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.8
Confidence interval	
level	95 %

sides	2-sided
lower limit	-0.8
upper limit	2.4

Notes:

[138] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[139]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	1.2

Notes:

[139] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[140]
Parameter estimate	Posterior adjacent median difference
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.3

Notes:

[140] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[141]
Parameter estimate	Posterior adjusted median difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.1
upper limit	1.1

Notes:

[141] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[142]
Parameter estimate	Posterior adjusted median difference
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	5.4

Notes:

[142] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[143]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.4

Notes:

[143] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[144]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	1.4

Notes:

[144] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 10

Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[145]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1

Notes:

[145] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[146]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	2.2

Notes:

[146] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analyis 12
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[147]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1

Notes:

[147] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[148]

Parameter estimate	Posterior adjusted median difference
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	5.1

Notes:

[148] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[149]
Parameter estimate	Posterior adjusted median difference
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2.8

Notes:

[149] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 15
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[150]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	1.1

Notes:

[150] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 84 was performed and posterior adjsted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[151]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided

lower limit	-1.9
upper limit	1.7

Notes:

[151] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 17
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[152]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2.8

Notes:

[152] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 18
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[153]
Parameter estimate	Posterior adjusted median difference
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.8
upper limit	1.7

Notes:

[153] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Secondary: Percentage of responders on the St. George's Respiratory Questionnaire (SGRQ) total score as measured by the SGRQ for COPD participants (SGRQ-C) at Days 28, 56, and 84

End point title	Percentage of responders on the St. George's Respiratory Questionnaire (SGRQ) total score as measured by the SGRQ for COPD participants (SGRQ-C) at Days 28, 56, and 84

End point description:

SGRQ-C is a 40-item questionnaire designed specifically to focus on COPD participants and was scored equivalent to the SGRQ Total Score, ranging from 0 to 100, where higher scores reflect worse health-related quality of life. The percentage of responders on the SGRQ Total Score was derived for participants with a Baseline SGRQ Total Score >=4. Percentage of responders on the SGRQ Total Score is defined as number of participants with a decrease from Baseline in SGRQ Total Score >=4 on or before Days 28, 56 and 84 divided by total number of participants in the MITT population. Analysis was performed using a separate Bayesian logistic regression for each time point adjusting for treatment group, smoking status at baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in the previous 12 months and gender. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:
Days 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[154]	22[155]	91[156]	92[157]
Units: Percentage of responders				
Day 28	21	14	19	26
Day 56	50	36	56	55
Day 84	61	50	66	63

Notes:
[154] - MITT Population.
[155] - MITT Population.
[156] - MITT Population.
[157] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[158]	89[159]	278[160]	
Units: Percentage of responders				
Day 28	32	24	21	
Day 56	60	49	53	
Day 84	68	57	62	

Notes:
[158] - MITT Population.
[159] - MITT Population.
[160] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[161]
Parameter estimate	Posterior median odds ratio
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	1.41

Notes:
[161] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg

Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[162]
Parameter estimate	Posterior median odds ratio
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	1.47

Notes:

[162] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[163]
Parameter estimate	Posterior median odds ratio
Point estimate	1.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	2.24

Notes:

[163] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[164]
Parameter estimate	Posterior median odds ratio
Point estimate	1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.91

Notes:

[164] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[165]

Parameter estimate	Posterior median odds ratio
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	2.08

Notes:

[165] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[166]
Parameter estimate	Posterior median odds ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.4

Notes:

[166] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[167]
Parameter estimate	Posterior median odds ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	1.16

Notes:

[167] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[168]
Parameter estimate	Posterior median odds ratio
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.74
upper limit	1.98

Notes:

[168] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[169]
Parameter estimate	Posterior median odds ratio
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.97

Notes:

[169] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 10
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[170]
Parameter estimate	Posterior median odds ratio
Point estimate	1.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	2.27

Notes:

[170] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[171]
Parameter estimate	Posterior median odds ratio
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.62

Notes:

[171] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 12
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[172]
Parameter estimate	Posterior median odds ratio
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.5

Notes:

[172] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[173]
Parameter estimate	Posterior median odds ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.39

Notes:

[173] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[174]
Parameter estimate	Posterior median odds ratio
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.72
upper limit	2.01

Notes:

[174] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 15

Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[175]
Parameter estimate	Posterior median odds ratio
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.79

Notes:

[175] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 84 was performed and posterior adjsted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[176]
Parameter estimate	Posterior median odds ratio
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.14

Notes:

[176] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 17
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[177]
Parameter estimate	Posterior median odds ratio
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.45

Notes:

[177] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 18
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[178]

Parameter estimate	Posterior median odds ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.43

Notes:

[178] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Secondary: Change from Baseline in SGRQ total score at Days 28, 56 and 84

End point title	Change from Baseline in SGRQ total score at Days 28, 56 and 84

End point description:

SGRQ-C is 40-item questionnaire was scored equivalent to SGRQ Total Score, ranging from 0-100, higher scores reflect worse health-related quality of life. Scores on a scale were calculated as 100*summed weights from positive items in questionnaire divided by sum of weights of all items in questionnaire. Baseline (Day 1) is latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline in SGRQ Total Score is SGRQ Total Score on Days 28, 56 and 84 minus Baseline SGRQ Total Score. Analysis was using Bayesian repeated measures model adjusting for Baseline by visit interaction, treatment by visit interaction, smoking status at Baseline, region, severity of index exacerbation, number of moderate/severe exacerbations in previous 12 months and gender. Posterior adjusted median change from Baseline and 95% HPD CrI was presented. Only those participants with data at specified data points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline and Days 28, 56 and 84

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[179]	22[180]	91[181]	92[182]
Units: Scores on a scale				
median (confidence interval 95%)				
Day 28, n=232, 19, 86, 78, 77, 72, 225	-7.7 (-9.8 to -5.7)	-5.7 (-12.2 to 0.5)	-8.2 (-11.4 to -5.1)	-10.6 (-13.8 to -7.1)
Day 56, n=227, 20, 78, 77, 74, 68, 219	-8.0 (-10.2 to -6.0)	-3.9 (-10.4 to 2.8)	-9.3 (-12.5 to -5.9)	-10.7 (-14.1 to -7.3)
Day 84, n=218, 17, 74, 74, 69, 60, 209	-9.1 (-11.3 to -6.8)	-6.6 (-13.6 to 0.3)	-9.3 (-12.8 to -6.0)	-11.3 (-14.8 to -7.7)

Notes:

[179] - MITT Population.

[180] - MITT Population.

[181] - MITT Population.

[182] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[183]	89[184]	278[185]	
Units: Scores on a scale				
median (confidence interval 95%)				

Day 28, n=232, 19, 86, 78, 77, 72, 225	-10.9 (-14.2 to -7.6)	-7.8 (-11.2 to -4.3)	-7.9 (-9.9 to -5.9)	
Day 56, n=227, 20, 78, 77, 74, 68, 219	-11.3 (-14.6 to -7.6)	-8.9 (-12.6 to -5.5)	-8.4 (-10.6 to -6.3)	
Day 84, n=218, 17, 74, 74, 69, 60, 209	-10.9 (-14.4 to -7.2)	-9.4 (-13.1 to -5.5)	-7.9 (-10.1 to -5.7)	

Notes:

[183] - MITT Population.

[184] - MITT Population.

[185] - MITT Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[186]
Parameter estimate	Posterior adjusted median difference
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	8.3

Notes:

[186] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 2
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[187]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3.1

Notes:

[187] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 3
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[188]
Parameter estimate	Posterior adjusted median difference
Point estimate	-2.9
Confidence interval	
level	95 %

sides	2-sided
lower limit	-6.2
upper limit	1.1

Notes:

[188] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 4
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[189]
Parameter estimate	Posterior adjusted median difference
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	0.4

Notes:

[189] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 5
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[190]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	3.5

Notes:

[190] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analyais 6
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[191]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	2.3

Notes:

[191] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 28 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 7
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[192]
Parameter estimate	Posterior adjusted median difference
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	11

Notes:

[192] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 8
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[193]
Parameter estimate	Posterior adjusted median difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	2.5

Notes:

[193] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 9
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[194]
Parameter estimate	Posterior adjusted median difference
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	1.1

Notes:

[194] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 10

Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[195]
Parameter estimate	Posterior adjusted median difference
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.3
upper limit	0.4

Notes:

[195] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 11
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[196]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	3

Notes:

[196] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 12
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[197]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	2.5

Notes:

[197] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 56 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 13
Comparison groups	Placebo v Nemiralisib 12.5 mcg
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	other[198]

Parameter estimate	Posterior adjusted median difference
Point estimate	2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.8
upper limit	9.4

Notes:

[198] - Treatment comparison between placebo and Nemiralisib 12.5 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 14
Comparison groups	Placebo v Nemiralisib 50 mcg
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	other[199]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	3.6

Notes:

[199] - Treatment comparison between placebo and Nemiralisib 50 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 15
Comparison groups	Placebo v Nemiralisib 100 mcg
Number of subjects included in analysis	368
Analysis specification	Pre-specified
Analysis type	other[200]
Parameter estimate	Posterior adjusted median difference
Point estimate	-2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	1.8

Notes:

[200] - Treatment comparison between placebo and Nemiralisib 100 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 16
Comparison groups	Placebo v Nemiralisib 250 mcg
Number of subjects included in analysis	366
Analysis specification	Pre-specified
Analysis type	other[201]
Parameter estimate	Posterior adjusted median difference
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided

lower limit	-5.7
upper limit	2.3

Notes:

[201] - Treatment comparison between placebo and Nemiralisib 250 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 17
Comparison groups	Placebo v Nemiralisib 500 mcg
Number of subjects included in analysis	365
Analysis specification	Pre-specified
Analysis type	other[202]
Parameter estimate	Posterior adjusted median difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.5
upper limit	3.8

Notes:

[202] - Treatment comparison between placebo and Nemiralisib 500 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Statistical analysis title	Statistical Analysis 18
Comparison groups	Placebo v Nemiralisib 750 mcg
Number of subjects included in analysis	554
Analysis specification	Pre-specified
Analysis type	other[203]
Parameter estimate	Posterior adjusted median difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	4

Notes:

[203] - Treatment comparison between placebo and Nemiralisib 750 mcg at Day 84 was performed and posterior adjusted median difference and 95% HPD CrI has been presented.

Secondary: Mean number of occasions of rescue medication use per day

End point title	Mean number of occasions of rescue medication use per day

End point description:

Albuterol (Salbutamol) MDI or nebules was used as a rescue medication. Rescue medication use was recorded as the number of occasions of rescue medication use each day. The mean number of occasions of rescue medication use per day is defined as sum of the number of occasions of rescue medication use each day within the time-period divided by the total number of days with non-missing values within the time-period. Over the 12-Week treatment period is defined as Day 1 to Day of last dose. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 of treatment and over the Week 12 treatment period

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[204]	22[205]	91[206]	92[207]
Units: No. of occasions of rescue use per day				
arithmetic mean (standard deviation)				
Week 1, n=254, 21, 87, 88, 80, 79, 254	1.699 (± 1.7674)	2.112 (± 2.2977)	1.633 (± 1.4320)	1.926 (± 2.1569)
Week 2, n=259, 21, 88, 89, 80, 82, 252	1.650 (± 1.8711)	2.231 (± 2.7169)	1.469 (± 1.4036)	1.712 (± 2.0310)
Week 3, n=256, 21, 90, 88, 80, 81, 245	1.729 (± 1.8157)	2.021 (± 2.2926)	1.495 (± 1.3943)	1.693 (± 1.9679)
Week 4, n=250, 21, 89, 87, 81, 77, 243	1.684 (± 1.7706)	2.190 (± 2.3657)	1.514 (± 1.5022)	1.720 (± 2.0083)
Week 5, n=251, 20, 88, 85, 78, 76, 240	1.735 (± 1.8662)	2.329 (± 2.6394)	1.533 (± 1.5706)	1.750 (± 2.0380)
Week 6, n=250, 20, 86, 84, 78, 72, 234	1.741 (± 1.9543)	2.378 (± 2.6904)	1.382 (± 1.4000)	1.792 (± 2.0822)
Week 7, n=250, 20, 85, 83, 77, 71, 231	1.703 (± 1.9914)	2.479 (± 2.6976)	1.531 (± 1.6374)	1.697 (± 2.0769)
Week 8, n=250, 20, 84, 83, 77, 71, 231	1.656 (± 1.8606)	2.736 (± 3.1579)	1.553 (± 1.5884)	1.616 (± 1.9444)
Week 9, n=244, 20, 82, 81, 76, 71, 229	1.708 (± 1.8709)	2.765 (± 3.1104)	1.608 (± 1.7699)	1.658 (± 2.0646)
Week 10, n=241, 20, 81, 80, 73, 71, 227	1.698 (± 1.9023)	2.543 (± 2.8753)	1.589 (± 1.6571)	1.596 (± 1.9809)
Week 11, n=241, 20, 79, 80, 73, 71, 226	1.729 (± 1.9406)	2.164 (± 2.2504)	1.404 (± 1.4897)	1.602 (± 1.9435)
Week 12, n=240, 20, 78, 80, 73, 70, 225	1.666 (± 1.7913)	2.386 (± 2.8157)	1.414 (± 1.3920)	1.671 (± 1.9612)
Over 12 Week, n=273, 21, 91, 91, 86, 83, 268	1.684 (± 1.6903)	2.330 (± 2.4715)	1.553 (± 1.4044)	1.750 (± 1.9048)

Notes:

[204] - MITT Population.

[205] - MITT Population.

[206] - MITT Population.

[207] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[208]	89[209]	278[210]	
Units: No. of occasions of rescue use per day				
arithmetic mean (standard deviation)				
Week 1, n=254, 21, 87, 88, 80, 79, 254	1.670 (± 1.5728)	1.917 (± 1.9298)	1.747 (± 1.7332)	
Week 2, n=259, 21, 88, 89, 80, 82, 252	1.497 (± 1.5700)	1.611 (± 1.7717)	1.587 (± 1.6531)	
Week 3, n=256, 21, 90, 88, 80, 81, 245	1.488 (± 1.6611)	1.742 (± 1.8380)	1.655 (± 1.7430)	
Week 4, n=250, 21, 89, 87, 81, 77, 243	1.489 (± 1.6734)	2.009 (± 2.0506)	1.707 (± 1.7512)	
Week 5, n=251, 20, 88, 85, 78, 76, 240	1.535 (± 1.8384)	1.949 (± 1.9685)	1.737 (± 1.8030)	
Week 6, n=250, 20, 86, 84, 78, 72, 234	1.636 (± 1.8042)	1.936 (± 2.0729)	1.780 (± 1.8083)	
Week 7, n=250, 20, 85, 83, 77, 71, 231	1.628 (± 1.8741)	1.899 (± 2.1694)	1.826 (± 1.8778)	

Week 8, n=250, 20, 84, 83, 77, 71, 231	1.572 (± 1.8294)	2.006 (± 2.2242)	1.824 (± 1.8397)	
Week 9, n=244, 20, 82, 81, 76, 71, 229	1.720 (± 1.8918)	1.953 (± 2.1838)	1.775 (± 1.8753)	
Week 10, n=241, 20, 81, 80, 73, 71, 227	1.546 (± 1.8824)	1.927 (± 2.1613)	1.705 (± 1.7646)	
Week 11, n=241, 20, 79, 80, 73, 71, 226	1.672 (± 1.9447)	1.926 (± 2.3243)	1.716 (± 1.7421)	
Week 12, n=240, 20, 78, 80, 73, 70, 225	1.712 (± 1.9532)	1.790 (± 2.1140)	1.731 (± 1.7245)	
Over 12 Week, n=273, 21, 91, 91, 86, 83, 268	1.620 (± 1.5994)	1.921 (± 1.9201)	1.733 (± 1.6618)	

Notes:

[208] - MITT Population.

[209] - MITT Population.

[210] - MITT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of rescue-free days

End point title	Percentage of rescue-free days

End point description:

Albuterol (Salbutamol) MDI or nebules was used as a rescue medication. Percentage of Rescue-Free Days is defined as sum of the number of days where the number of occasions of rescue medication use is zero within the time-period divided by total number of days with non-missing values within the time-period multiplied by 100 where the time-period is defined as follows: Week 1: Day 1-7; Week 2: Day 8 - 14; Week 3: Day 15-21; Week 4: Day 22-28; Week 5: Day 29-35; Week 6: Day 36-42; Week 7: Day 43-49; Week 8: Day 50-56; Week 9: Day 57-63; Week 10: Day 64-70; Week 11: Day 71-77; Week 12: Day 78 to Day of last dose; Over the 12-Week: Day 1 to Day of last dose. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Weeks 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 of treatment and over the Week 12 treatment period

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[211]	22[212]	91[213]	92[214]
Units: Percentage of rescue free days				
arithmetic mean (standard deviation)				
Week 1, n=254, 21, 87, 88, 80, 79, 254	34.898 (± 37.7118)	36.076 (± 44.3182)	29.849 (± 38.3385)	33.392 (± 39.7372)
Week 2, n=259, 21, 88, 89, 80, 82, 252	41.002 (± 40.9566)	40.819 (± 46.7899)	32.145 (± 41.2227)	43.017 (± 43.9884)
Week 3, n=256, 21, 90, 88, 80, 81, 245	38.204 (± 39.0621)	38.776 (± 44.0612)	31.643 (± 38.0943)	39.964 (± 40.3936)
Week 4, n=250, 21, 89, 87, 81, 77, 243	39.678 (± 40.8359)	35.376 (± 43.9405)	32.531 (± 39.0078)	42.202 (± 43.0692)
Week 5, n=251, 20, 88, 85, 78, 76, 240	38.262 (± 40.7807)	35.005 (± 41.8344)	35.552 (± 40.5745)	41.682 (± 41.3648)
Week 6, n=250, 20, 86, 84, 78, 72, 234	40.287 (± 42.2167)	37.870 (± 40.2125)	35.384 (± 40.9175)	41.720 (± 44.0117)
Week 7, n=250, 20, 85, 83, 77, 71, 231	41.373 (± 43.4266)	32.145 (± 43.1992)	35.634 (± 41.3319)	45.266 (± 43.5910)

Week 8, n=250, 20, 84, 83, 77, 71, 231	42.058 (± 41.2168)	34.290 (± 42.8300)	33.029 (± 41.0867)	44.118 (± 41.6682)
Week 9, n=244, 20, 82, 81, 76, 71, 229	39.268 (± 40.5300)	32.145 (± 44.6657)	32.759 (± 39.2972)	42.505 (± 41.2121)
Week 10, n=241, 20, 81, 80, 73, 71, 227	40.608 (± 41.0492)	35.000 (± 42.3430)	32.456 (± 40.7192)	43.396 (± 42.3040)
Week 11, n=241, 20, 79, 80, 73, 71, 226	39.701 (± 41.9689)	38.575 (± 44.2366)	35.624 (± 42.6625)	42.859 (± 41.7845)
Week 12, n=240, 20, 78, 80, 73, 70, 225	41.390 (± 40.8871)	39.415 (± 45.0442)	37.369 (± 40.2613)	41.300 (± 39.8199)
Over 12 Week, n=273, 21, 91, 91, 86, 83, 268	39.743 (± 36.8957)	35.533 (± 39.0694)	33.590 (± 36.6456)	40.441 (± 37.6285)

Notes:

[211] - MITT Population.

[212] - MITT Population.

[213] - MITT Population.

[214] - MITT Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[215]	89[216]	278[217]	
Units: Percentage of rescue free days				
arithmetic mean (standard deviation)				
Week 1, n=254, 21, 87, 88, 80, 79, 254	32.583 (± 38.3577)	34.453 (± 35.9802)	29.779 (± 36.1498)	
Week 2, n=259, 21, 88, 89, 80, 82, 252	38.573 (± 40.3629)	40.595 (± 41.1717)	33.639 (± 38.9767)	
Week 3, n=256, 21, 90, 88, 80, 81, 245	41.191 (± 42.1751)	34.923 (± 40.4026)	33.006 (± 38.4986)	
Week 4, n=250, 21, 89, 87, 81, 77, 243	43.194 (± 41.0201)	30.986 (± 38.5941)	32.394 (± 39.0174)	
Week 5, n=251, 20, 88, 85, 78, 76, 240	41.026 (± 42.1584)	33.912 (± 37.9973)	33.168 (± 39.0654)	
Week 6, n=250, 20, 86, 84, 78, 72, 234	39.196 (± 41.6575)	35.519 (± 42.2122)	32.351 (± 39.2542)	
Week 7, n=250, 20, 85, 83, 77, 71, 231	40.409 (± 42.0560)	38.232 (± 41.0296)	31.975 (± 39.4910)	
Week 8, n=250, 20, 84, 83, 77, 71, 231	42.918 (± 42.8354)	34.811 (± 39.3585)	32.357 (± 39.9221)	
Week 9, n=244, 20, 82, 81, 76, 71, 229	39.476 (± 42.2376)	36.823 (± 42.3513)	33.606 (± 39.4690)	
Week 10, n=241, 20, 81, 80, 73, 71, 227	41.492 (± 42.1984)	37.024 (± 41.2291)	33.483 (± 40.1924)	
Week 11, n=241, 20, 79, 80, 73, 71, 226	39.337 (± 42.3061)	39.841 (± 43.7237)	33.127 (± 39.1842)	
Week 12, n=240, 20, 78, 80, 73, 70, 225	39.981 (± 40.8296)	42.236 (± 42.1567)	33.906 (± 38.4851)	
Over 12 Week, n=273, 21, 91, 91, 86, 83, 268	39.631 (± 36.5157)	35.820 (± 34.6377)	32.743 (± 33.9362)	

Notes:

[215] - MITT Population.

[216] - MITT Population.

[217] - MITT Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of Nemiralisib

End point title	Plasma concentration of Nemiralisib[218]

End point description:

Plasma samples were collected at indicated time points and analyzed for concentrations of Nemiralisb. Pharmacokinetic (PK) Population consists of all participants in the Safety population who had at least 1 non-missing PK assessment (Non-quantifiable [NQ] values will be considered as non-missing values). Participants were summarized according to the treatment that they actually received. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[218] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[219]	22[220]	24[221]	19[222]
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)				
Day 14, Pre-dose, n=2, 19, 24, 16, 18, 69	113.6 (± 6)	62.0 (± 46)	142.8 (± 44)	416.0 (± 59)
Day 14, 0-1 hour, n=4, 19, 24, 15, 18, 67	54.9 (± 43)	109.9 (± 51)	253.7 (± 73)	767.6 (± 71)
Day 14, >1-6 hours, n=4, 20, 23, 15, 18, 65	35.0 (± 57)	93.1 (± 58)	231.8 (± 53)	657.0 (± 61)
Day 28, Pre-dose, n=2, 18, 23, 16, 16, 67	23.6 (± 24)	60.5 (± 45)	129.4 (± 46)	315.6 (± 85)
Day 28, 0-1 hour, n=3, 19, 23, 16, 15, 63	36.2 (± 26)	104.9 (± 70)	253.3 (± 52)	807.0 (± 66)
Day 28, >1-6 hours, n=3, 18, 23, 16, 14, 64	28.1 (± 15)	85.4 (± 40)	211.4 (± 41)	598.8 (± 39)

Notes:

[219] - PK Population.

[220] - PK Population.

[221] - PK Population.

[222] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[223]	73[224]		
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)				
Day 14, Pre-dose, n=2, 19, 24, 16, 18, 69	687.3 (± 53)	1069.6 (± 70)		
Day 14, 0-1 hour, n=4, 19, 24, 15, 18, 67	1492.0 (± 59)	1972.0 (± 110)		
Day 14, >1-6 hours, n=4, 20, 23, 15, 18, 65	1146.7 (± 56)	1622.7 (± 90)		
Day 28, Pre-dose, n=2, 18, 23, 16, 16, 67	528.3 (± 110)	937.6 (± 101)		

Day 28, 0-1 hour, n=3, 19, 23, 16, 15, 63	1552.2 (± 83)	1717.6 (± 114)		
Day 28, >1-6 hours, n=3, 18, 23, 16, 14, 64	1079.5 (± 80)	1388.1 (± 101)		

Notes:

[223] - PK Population.

[224] - PK Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting non-serious adverse events (non-SAEs), SAEs and AE of special interest (AESI)

End point title	Number of participants reporting non-serious adverse events (non-SAEs), SAEs and AE of special interest (AESI)

End point description:

An AE is any untoward medical occurrence in a clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is defined as any untoward medical occurrence that, at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability, is a congenital anomaly/ birth effect and other important medical events. Safety Population consists of all randomized participants who received at least one dose of study treatment. Participants were summarized according to treatment that they actually received.

End point type	Secondary

End point timeframe:

Up to Week 24

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[225]	22[226]	91[227]	92[228]
Units: Participants				
Any non-SAE	31	1	14	19
Any SAE	23	2	9	13
Any AESI	9	0	10	10

Notes:

[225] - Safety Population.

[226] - Safety Population.

[227] - Safety Population.

[228] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[229]	89[230]	278[231]	
Units: Participants				
Any non-SAE	25	36	101	
Any SAE	16	6	26	
Any AESI	21	29	93	

Notes:

[229] - Safety Population.

[230] - Safety Population.

[231] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case post Baseline diastolic blood pressure (DBP), systolic blood pressure (SBP) and pulse rate

End point title	Number of participants with worst case post Baseline diastolic blood pressure (DBP), systolic blood pressure (SBP) and pulse rate

End point description:

The DBP, SBP and pulse rate were measured with participants seated at least 5 minutes before the assessments. Participants are counted in the worst case category if their value changes to (low, within range or no change, or high). Participants whose value category was unchanged (e.g., High to High), or whose value became within range, are recorded in the "To w/in Range or No Change" category. Participants are counted twice if the participant has values that changed "To Low" and "To High", so the percentages may not add to 100%. Participants with missing baseline value are assumed to have within range value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 16

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	271[232]	21[233]	91[234]	92[235]
Units: Participants				
DBP, To low	8	3	3	0
DBP, To within range/no change	260	17	85	91
DBP, To high	3	1	3	1
Pulse rate, To low	1	0	0	0
Pulse rate,To within range/no change	265	21	84	90
Pulse rate, To high	5	0	7	2
SBP, To low	11	1	5	3
SBP, To withinn range/no change	250	18	83	82
SBP, To high	10	2	3	7

Notes:

[232] - Safety Population.

[233] - Safety Population.

[234] - Safety Population.

[235] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	88[236]	88[237]	266[238]	

Units: Participants				
DBP, To low	4	4	7	
DBP, To within range/no change	79	82	256	
DBP, To high	5	2	3	
Pulse rate, To low	0	0	0	
Pulse rate,To within range/no change	82	83	258	
Pulse rate, To high	6	5	8	
SBP, To low	2	3	8	
SBP, To withinn range/no change	79	80	239	
SBP, To high	8	6	19	

Notes:

[236] - Safety Population.

[237] - Safety Population.

[238] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal electrocardiogram (ECG) findings

End point title	Number of participants with abnormal electrocardiogram (ECG) findings

End point description:

A single 12-lead ECG with a 15-second rhythm strip was obtained using an ECG machine that automatically calculated the heart rate and measured PR, QRS, QT and corrected QT (QTc) intervals. Abnormal ECG findings are presented.

End point type	Secondary

End point timeframe:

Screening, Days 14, 84, 112 and at early withdrawal

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[239]	22[240]	91[241]	92[242]
Units: Participants				
Screening	93	10	25	37
Day 14	88	8	24	33
Day 84	79	8	22	27
Day 112	77	11	28	28
Early withdrawal	3	0	2	1

Notes:

[239] - Safety Population.

[240] - Safety Population.

[241] - Safety Population.

[242] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[243]	89[244]	278[245]	
Units: Participants				

Screening	28	21	86	
Day 14	29	18	74	
Day 84	24	18	64	
Day 112	25	20	75	
Early withdrawal	3	1	4	

Notes:

[243] - Safety Population.

[244] - Safety Population.

[245] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case post Baseline clinical chemistry values

End point title	Number of participants with worst case post Baseline clinical chemistry values

End point description:

Blood samples were collected for the analysis of clinical chemistry parameters including: blood urea nitrogen (BUN), creatinine (Crt), glucose (Glu), potassium (Pot), sodium (Sod), calcium (Cal), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total and direct bilirubin, total protein and albumin (Alb). Participants are counted in the worst case category if their value changes to (low, within range or no change, or high). Participants whose value category was unchanged (e.g., High to High), or whose value became within range, are recorded in the "To w/in Range or No Change" category. Participants are counted twice if the participant has values that changed "To Low" and "To High", so the percentages may not add to 100%. Participants with missing baseline value are assumed to have within range value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Upto Week 16

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[246]	22[247]	91[248]	92[249]
Units: Participants				
Alb,To low, n=266, 21, 91, 90, 87, 85, 263	2	0	0	0
Alb,w/in range/no change,n=266,21,91,90,87,85,263	264	21	90	90
Alb,To high,n=266,21,91,90,87,85,263	0	0	1	0
Cal,To low, n=266, 21, 90, 90, 87, 85, 263	1	0	0	0
Cal,w/in range/no change,n=266,21,90,90,87,85,263	265	21	90	90
Cal,To high, n=266,21,90,90,87,85,263	0	0	0	0
Crt,To low, n=266, 21, 91, 90, 87, 85, 263	27	3	10	7
Crt,w/in range/no change,n=266,21,91,90,87,85,263	237	18	81	82
Crt,To high, n=266,21,91,90,87,85,263	2	0	0	1
Glu,To low, n=266, 21, 91, 90, 87, 85, 263	0	0	0	1

Glu,w/in range/no change,n=266,21,91,90,87,85,263	266	21	91	89
Glu,To high, n=266,21,91,90,87,85,263	0	0	0	0
Pot,To low, n=266, 21, 90, 90, 87, 85, 263	0	0	0	0
Pot,w/in range/no change,n=266,21,90,90,87,85,263	264	21	90	90
Pot,To high, n=266,21,90,90,87,85,263	2	0	0	0
Sod,To low, n=266, 21, 91, 90, 87, 85, 263	0	0	0	0
Sod,w/in range/no change,n=266,21,91,90,87,85,263	266	21	91	90
Sod,To high, n=266,21,91,90,87,85,263	0	0	0	0
BUN,To low, n=266, 21, 91, 90, 87, 85, 263	7	0	3	2
BUN,w/in range/no change,n=266,21,91,90,87,85,263	256	21	88	86
BUN,To high, n=266,21,91,90,87,85,263	3	0	0	2

Notes:

[246] - Safety Population.

[247] - Safety Population.

[248] - Safety Population.

[249] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[250]	89[251]	278[252]	
Units: Participants				
Alb,To low, n=266, 21, 91, 90, 87, 85, 263	1	1	2	
Alb,w/in range/no change,n=266,21,91,90,87,85,263	85	84	261	
Alb,To high,n=266,21,91,90,87,85,263	1	0	0	
Cal,To low, n=266, 21, 90, 90, 87, 85, 263	0	1	1	
Cal,w/in range/no change,n=266,21,90,90,87,85,263	87	84	262	
Cal,To high, n=266,21,90,90,87,85,263	0	0	0	
Crt,To low, n=266, 21, 91, 90, 87, 85, 263	4	9	32	
Crt,w/in range/no change,n=266,21,91,90,87,85,263	80	76	231	
Crt,To high, n=266,21,91,90,87,85,263	3	0	0	
Glu,To low, n=266, 21, 91, 90, 87, 85, 263	0	0	0	
Glu,w/in range/no change,n=266,21,91,90,87,85,263	87	85	263	
Glu,To high, n=266,21,91,90,87,85,263	0	0	0	
Pot,To low, n=266, 21, 90, 90, 87, 85, 263	0	0	0	
Pot,w/in range/no change,n=266,21,90,90,87,85,263	86	84	262	
Pot,To high, n=266,21,90,90,87,85,263	1	1	1	
Sod,To low, n=266, 21, 91, 90, 87, 85, 263	0	0	0	
Sod,w/in range/no change,n=266,21,91,90,87,85,263	87	85	263	

Sod,To high, n=266,21,91,90,87,85,263	0	0	0	
BUN,To low, n=266, 21, 91, 90, 87, 85, 263	2	3	6	
BUN,w/in range/no change,n=266,21,91,90,87,85,263	85	82	253	
BUN,To high, n=266,21,91,90,87,85,263	0	0	4	

Notes:

[250] - Safety Population.

[251] - Safety Population.

[252] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case post Baseline hematology values

End point title	Number of participants with worst case post Baseline hematology values

End point description:

Blood samples were collected for the analysis of hematology parameters including: platelets (Pla), red blood cells count, Hemoglobin (Hb), Hematocrit, mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), percentage reticulocytes, neutrophils (Neu), lymphocytes (Lym), monocytes, eosinophils, leukocytes (Leu) and basophils. Participants are counted in the worst case category if their value changes to (low, within range or no change, or high). Participants whose value category was unchanged (e.g., High to High), or whose value became within range, are recorded in the "To w/in Range or No Change" category. Participants are counted twice if the participant has values that changed "To Low" and "To High", so the percentages may not add to 100%. Participants with missing baseline value are assumed to have within range value. Only those participants with data available at the specified data points were analyzed (represented by n= X in the category titles).

End point type	Secondary

End point timeframe:

Upto Week 16

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[253]	22[254]	91[255]	92[256]
Units: Participants				
Hb,To low, n=260, 20, 90, 90, 84, 81, 254	0	0	0	0
Hb,w/in range/no change,n=260,20,90,90,84,81,254	260	20	90	90
Hb,To high,n=260, 20, 90, 90, 84, 81, 254	0	0	0	0
Leu,To low,n=259, 20, 90, 90, 83, 78, 251	0	0	0	0
Leu,w/in range/no change,n=259,20,90,90,83,78,251	211	16	81	74
Leu,To high, n=259,20,90,90,83,78,251	48	4	9	16
Lym,To low, n=256, 20, 85, 88, 82, 77, 249	8	1	6	7
Lym,w/in range/no change,n=256,20,85,88,82,77,249	239	19	79	76
Lym,To high,n=256,20,85,88,82,77,249	9	0	0	5

Neu, To low, n=256,20,85,88,82,77,249	3	0	1	1
Neu,w/in range/no change,n=256,20,85,88,82,77,249	215	17	73	76
Neu,To high, n=256,20,85,88,82,77,249	38	3	11	11
Pla,To low, n=253, 19, 88, 90, 84, 78, 245	0	0	0	0
Pla,w/in range/no change,n=253,19,88,90,84,78,245	253	19	88	90
Pla,To high, n=253,19,88,90,84,78,245	0	0	0	0

Notes:

[253] - Safety Population.

[254] - Safety Population.

[255] - Safety Population.

[256] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[257]	89[258]	278[259]	
Units: Participants				
Hb,To low, n=260, 20, 90, 90, 84, 81, 254	0	0	0	
Hb,w/in range/no change,n=260,20,90,90,84,81,254	84	81	253	
Hb,To high,n=260, 20, 90, 90, 84, 81, 254	0	0	1	
Leu,To low,n=259, 20, 90, 90, 83, 78, 251	0	0	0	
Leu,w/in range/no change,n=259,20,90,90,83,78,251	63	62	201	
Leu,To high, n=259,20,90,90,83,78,251	20	16	50	
Lym,To low, n=256, 20, 85, 88, 82, 77, 249	7	2	11	
Lym,w/in range/no change,n=256,20,85,88,82,77,249	70	73	226	
Lym,To high,n=256,20,85,88,82,77,249	5	2	12	
Neu, To low, n=256,20,85,88,82,77,249	0	0	2	
Neu,w/in range/no change,n=256,20,85,88,82,77,249	68	60	213	
Neu,To high, n=256,20,85,88,82,77,249	14	17	34	
Pla,To low, n=253, 19, 88, 90, 84, 78, 245	0	0	0	
Pla,w/in range/no change,n=253,19,88,90,84,78,245	84	78	245	
Pla,To high, n=253,19,88,90,84,78,245	0	0	0	

Notes:

[257] - Safety Population.

[258] - Safety Population.

[259] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants reporting COPD exacerbations

End point title	Number of participants reporting COPD exacerbations

End point description:

Participants reporting acute COPD exacerbations during the study period has been presented.

End point type	Secondary

End point timeframe:

Up to Week 16

End point values	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	276[260]	22[261]	91[262]	92[263]
Units: Participants	8	1	6	4

Notes:

[260] - Safety Population.

[261] - Safety Population.

[262] - Safety Population.

[263] - Safety Population.

End point values	Nemiralisib 250 mcg	Nemiralisib 500 mcg	Nemiralisib 750 mcg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	90[264]	89[265]	278[266]	
Units: Participants	4	3	17	

Notes:

[264] - Safety Population.

[265] - Safety Population.

[266] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Area under the concentration time curve (AUC) from time zero to 24 hours [AUC(0-24)] of nemiralisib

End point title	Area under the concentration time curve (AUC) from time zero to 24 hours [AUC(0-24)] of nemiralisib[267]

End point description:

Plasma samples were collected at indicated time points and analyzed. This was a conditional secondary endpoint for which results are not available because development of GSK2269557 was terminated and therefore secondary population pharmacokinetic (Pop PK) analyses were not conducted.

End point type	Other pre-specified

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[267] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[268]	22[269]	24[270]	19[271]
Units: Hours*picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Notes:

[268] - PK Population.

[269] - PK Population.

[270] - PK Population.

[271] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[272]	73[273]		
Units: Hours*picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)		

Notes:

[272] - PK Population.

[273] - PK Population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: AUC from time zero to time 't' [AUC(0-t)] of nemiralisib

End point title	AUC from time zero to time 't' [AUC(0-t)] of nemiralisib[274]

End point description:

Plasma samples were collected at indicated time points and analyzed. This was a conditional secondary endpoint for which results are not available because development of GSK2269557 was terminated and therefore secondary Pop PK analyses were not conducted.

End point type	Other pre-specified

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[274] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[275]	22[276]	24[277]	19[278]
Units: Hours*picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Notes:

[275] - PK Population.

[276] - PK Population.

[277] - PK Population.

[278] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[279]	73[280]		
Units: Hours*picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)		

Notes:

[279] - PK Population.

[280] - PK Population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Maximum Observed Plasma Drug Concentration (Cmax) of nemiralisib

End point title	Maximum Observed Plasma Drug Concentration (Cmax) of nemiralisib[281]

End point description:

Plasma samples were collected at indicated time points and analyzed. This was a conditional secondary endpoint for which results are not available because development of GSK2269557 was terminated and therefore secondary Pop PK analyses were not conducted.

End point type	Other pre-specified

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[281] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[282]	22[283]	24[284]	19[285]
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Notes:

[282] - PK Population.

[283] - PK Population.

[284] - PK Population.

[285] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[286]	73[287]		
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)		

Notes:

[286] - PK Population.

[287] - PK Population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Time to reach Cmax (Tmax) of nemiralisib

End point title	Time to reach Cmax (Tmax) of nemiralisib[288]

End point description:

Plasma samples were collected at indicated time points and analyzed. This was a conditional secondary endpoint for which results are not available because development of GSK2269557 was terminated and therefore secondary Pop PK analyses were not conducted.

End point type	Other pre-specified

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[288] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[289]	22[290]	24[291]	19[292]
Units: Hours				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Notes:

[289] - PK Population.

[290] - PK Population.

[291] - PK Population.

[292] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[293]	73[294]		
Units: Hours				
median (full range (min-max))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Notes:

[293] - PK Population.

[294] - PK Population.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Plasma drug concentration at pre-dose (Ctrough) of nemiralisib

End point title	Plasma drug concentration at pre-dose (Ctrough) of

End point description:

Plasma samples were collected at indicated time points and analyzed. This was a conditional secondary endpoint for which results are not available because development of GSK2269557 was terminated and therefore secondary Pop PK analyses were not conducted.

End point type	Other pre-specified

End point timeframe:

Pre-dose, 0-1 hour, >1-6 hours post-dose on Days 14 and 28

Notes:

[295] - 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: Plasma concentration was analyzed for the active comparator, Nemiralisib.

End point values	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg	Nemiralisib 100 mcg	Nemiralisib 250 mcg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5[296]	22[297]	24[298]	19[299]
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Notes:

[296] - PK Population.

[297] - PK Population.

[298] - PK Population.

[299] - PK Population.

End point values	Nemiralisib 500 mcg	Nemiralisib 750 mcg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20[300]	73[301]		
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)	99999 (± 99999)	99999 (± 99999)		

Notes:

[300] - PK Population.

[301] - PK Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-serious AEs and SAEs were collected up to Week 24

Adverse event reporting additional description:

Non-serious AEs and SAEs were summarized for the Safety Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants were administered a single oral inhalation of placebo via ELLIPTA dry powder inhaler (DPI) once daily in the morning for 12 weeks. Albuterol (salbutamol) metered-dose inhaler (MDI) or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 12.5 mcg

Reporting group description:

Participants were administered a single oral inhalation of 12.5 micrograms (mcg) nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 50 mcg

Reporting group description:

Participants were administered a single oral inhalation of 50 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 100 mcg

Reporting group description:

Participants were administered a single oral inhalation of 100 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 250 mcg

Reporting group description:

Participants were administered a single oral inhalation of 250 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 500 mcg

Reporting group description:

Participants were administered a single oral inhalation of 500 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Reporting group title	Nemiralisib 750 mcg

Reporting group description:

Participants were administered a single oral inhalation of 750 mcg nemiralisib via ELLIPTA DPI once daily in the morning for 12 weeks. Albuterol (salbutamol) MDI or nebules were also provided to all participants as rescue medication.

Serious adverse events	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 276 (8.33%)	2 / 22 (9.09%)	9 / 91 (9.89%)
number of deaths (all causes)	1	0	3
number of deaths resulting from adverse events			
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bronchial carcinoma			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine tumour			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			

subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			

subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrhythmia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chroni obstructive pulmonary disease			

subjects affected / exposed	8 / 276 (2.90%)	1 / 22 (4.55%)	6 / 91 (6.59%)
occurrences causally related to treatment / all	1 / 8	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)

occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial hematoma			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocele			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 276 (0.00%)	1 / 22 (4.55%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 276 (0.00%)	1 / 22 (4.55%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	4 / 276 (1.45%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis klebsiella			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 276 (0.00%)	0 / 22 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 276 (0.36%)	0 / 22 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Nemiralisib 100 mcg	Nemiralisib 250 mcg	Nemiralisib 500 mcg
Total subjects affected by serious adverse events			

subjects affected / exposed	13 / 92 (14.13%)	16 / 90 (17.78%)	6 / 89 (6.74%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bronchial carcinoma			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma of colon			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine tumour			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)

occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Swelling			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Conversion disorder			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 92 (1.09%)	2 / 90 (2.22%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Atrioventricular block			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrhythmia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chroni obstructive pulmonary disease			
subjects affected / exposed	4 / 92 (4.35%)	4 / 90 (4.44%)	3 / 89 (3.37%)
occurrences causally related to treatment / all	0 / 4	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Acute respiratory failure			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)

occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial hematoma			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Enterocele			
subjects affected / exposed	0 / 92 (0.00%)	1 / 90 (1.11%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bile duct stone			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic acidosis			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 92 (2.17%)	3 / 90 (3.33%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 92 (1.09%)	1 / 90 (1.11%)	0 / 89 (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
Diverticulitis			
subjects affected / exposed	1 / 92 (1.09%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis klebsiella			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 92 (0.00%)	0 / 90 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Nemiralisib 750 mcg		
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 278 (9.35%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	0 / 278 (0.00%)		

occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Bronchial carcinoma				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adenocarcinoma of colon				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuroendocrine tumour				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				

Non-cardiac chest pain				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Swelling				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Conversion disorder				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Contusion				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			

deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-reactive protein increased				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Angina unstable				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			

deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Sinus arrhythmia				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Chroni obstructive pulmonary disease				
subjects affected / exposed	17 / 278 (6.12%)			
occurrences causally related to treatment / all	1 / 17			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			

deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				
subjects affected / exposed	1 / 278 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wheezing				
subjects affected / exposed	0 / 278 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Intracranial hematoma			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Enterocele			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematochezia			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis acute			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct stone			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		

deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal impairment			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 278 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystitis klebsiella			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 278 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	Nemiralisib 12.5 mcg	Nemiralisib 50 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 276 (11.23%)	1 / 22 (4.55%)	14 / 91 (15.38%)
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	13 / 276 (4.71%)	0 / 22 (0.00%)	10 / 91 (10.99%)
occurrences (all)	13	0	12

Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 276 (0.72%) 2	0 / 22 (0.00%) 0	0 / 91 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	23 / 276 (8.33%) 41	1 / 22 (4.55%) 1	6 / 91 (6.59%) 8

Non-serious adverse events	Nemiralisib 100 mcg	Nemiralisib 250 mcg	Nemiralisib 500 mcg
Total subjects affected by non-serious adverse events subjects affected / exposed	19 / 92 (20.65%)	25 / 90 (27.78%)	36 / 89 (40.45%)
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	11 / 92 (11.96%) 17	23 / 90 (25.56%) 27	31 / 89 (34.83%) 58
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 92 (2.17%) 2	3 / 90 (3.33%) 3	5 / 89 (5.62%) 5
Nervous system disorders Headache subjects affected / exposed occurrences (all)	8 / 92 (8.70%) 10	4 / 90 (4.44%) 5	2 / 89 (2.25%) 2

Non-serious adverse events	Nemiralisib 750 mcg		
Total subjects affected by non-serious adverse events subjects affected / exposed	101 / 278 (36.33%)		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	96 / 278 (34.53%) 141		
Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 278 (0.72%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	15 / 278 (5.40%) 18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 September 2017	Amendment 01: Updated and clarified the protocol during the Voluntary Harmonization Procedure in the European Union (EU).
14 December 2017	Amendment 02: Added the 12.5 mcg nemiralisib dose, added the provision for a 25 mcg dose to be added later, removed restrictions on theophylline use, made changes to discontinuation criteria, clarified the protocol, corrected minor discrepancies, and changed serious adverse events (SAE) recording such that SAEs prior to the start of study treatment were only collected if they were considered related to study participation or a GSK product.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported