Clinical trial results:
A randomised, double-blind, placebo-controlled study to evaluate the safety, efficacy and changes in induced sputum and blood biomarkers following daily repeat doses of inhaled GSK2269557 for 12 weeks in adult subjects diagnosed with an acute exacerbation of Chronic Obstructive Pulmonary Disease (COPD).

Summary

EudraCT number	2015-003696-30
Trial protocol	DK
Global end of trial date	22 June 2018

Results information

Result version number	v1
This version publication date	28 June 2019
First version publication date	28 June 2019

Trial information

Trial identification

Sponsor protocol code	201928

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,
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	31 January 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 June 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To establish the PI3K δ-dependent changes in previously identified immune cell mechanisms specifically related to neutrophil function using mRNA in sputum from participants with an exacerbation of COPD, with or without treatment with GSK2269557.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2015
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	Canada: 33
Country: Number of subjects enrolled	Denmark: 11
Worldwide total number of subjects	44
EEA total number of subjects	11

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)	23
From 65 to 84 years	21
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total 44 participants with Chronic obstructive pulmonary disease (COPD) were enrolled in this study. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA.but the 2 treatment arms remained the same i.e. Placebo and GSK2269557 (Nemiralisib [NEMI]).There was no intent to compare two devices.

Pre-assignment

Screening details:

As the switch to the ELLIPTA device was intended to be a comparable treatment, the treatment groups Placebo DISKUS and Placebo ELLIPTA were combined as All Placebo treatment group. Similarly, the treatment groups NEMI DISKUS and NEMI ELLIPTA were combined as All NEMI treatment group.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	All Placebo

Arm description:

Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS or ELLIPTA dry powder inhaler (DPI).

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:

Lactose was administered using a DISKUS or ELLIPTA dry powder inhaler device.

Arm title	All NEMI

Arm description:

Participants were administered with either NEMI 1000 micrograms (mcg) once daily in the morning using DISKUS DPI or 700 mcg once daily in the morning using ELLIPTA DPI before breakfast for 84 consecutive days

Arm type	Experimental
Investigational medicinal product name	GSK2269557
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

GSK2269557 500 mcg blended with lactose was administered using a DISKUS dry powder inhaler device or as 700 mcg once daily for 84 consecutive days via ELLIPTA dry powder inhaler device.

Number of subjects in period 1	All Placebo	All NEMI
Started	22	22
Completed	18	21
Not completed	4	1
Consent withdrawn by subject	2	-
Physician decision	-	1
Adverse event, non-fatal	2	-

Baseline characteristics

Reporting groups	
Reporting group title	All Placebo
Reporting group description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS or ELLIPTA dry powder inhaler (DPI).	
Reporting group title	All NEMI
Reporting group description:	
Participants were administered with either NEMI 1000 micrograms (mcg) once daily in the morning using DISKUS DPI or 700 mcg once daily in the morning using ELLIPTA DPI before breakfast for 84 consecutive days	

Reporting group values	All Placebo	All NEMI	Total
Number of subjects	22	22	44
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)	13	10	23
From 65-84 years	9	12	21
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	64.0	66.1	
standard deviation	± 8.20	± 7.32	-
Sex: Female, Male			
Units: Subjects			
Female	10	11	21
Male	12	11	23
Race/Ethnicity, Customized			
Units: Subjects			
White - White/Caucasian/European Heritage	22	22	44

End points

End points reporting groups

Reporting group title	All Placebo
Reporting group description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS or ELLIPTA dry powder inhaler (DPI).	
Reporting group title	All NEMI
Reporting group description:	
Participants were administered with either NEMI 1000 micrograms (mcg) once daily in the morning using DISKUS DPI or 700 mcg once daily in the morning using ELLIPTA DPI before breakfast for 84 consecutive days	
Subject analysis set title	All NEMI/All Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
This arm is a comparison of All NEMI and All Placebo Arm	
Subject analysis set title	Placebo via DISKUS
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI.	
Subject analysis set title	NEMI 1000 mcg via DISKUS
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with NEMI 1000 mcg once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI.	
Subject analysis set title	Placebo via ELLIPTA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI.	
Subject analysis set title	NEMI 700 mcg via ELLIPTA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with NEMI 700 mcg once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI.	
Subject analysis set title	Placebo via DISKUS
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI	
Subject analysis set title	Placebo via ELLIPTA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI	
Subject analysis set title	NEMI 700 mcg via ELLIPTA
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were administered with NEMI 700 mcg once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI	
Subject analysis set title	NEMI 1000 mcg via DISKUS
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered with NEMI 1000 mcg once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI

Subject analysis set title	NEMI 700 mcg via ELLIPTA
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered with NEMI 700 mcg once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI

Primary: Change in Messenger Ribonucleic acid (mRNA) transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in NEMI treatment group

End point title	Change in Messenger Ribonucleic acid (mRNA) transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in NEMI treatment group[1][2]

End point description:

Saline-induced sputum samples were collected at the indicated time-points to determine the alterations in previously identified immune cell mechanisms specifically related to neutrophil function by identifying the changes in mRNA transcriptome in induced sputum. Baseline was defined as screening visit. The log2 transformed mRNA intensities for each probe set were analyzed in a separate repeated measures model. Back transformed baseline-adjusted ratios and two-sided unadjusted p-values were calculated for each visit as the specified time-point value/baseline value. These ratios were converted to fold change values; if ratio >= 1 then fold change=ratio or if ratio < 1 then fold change = -1/ratio. Data for pre-specified probe sets that meet the criteria fold change >1.5 or <-1.5 and p<0.05 for All NEMI group is presented. In the categories column we have included time-point, Probe ID and Gene label.

End point type	Primary

End point timeframe:

Baseline (Screening) and Days 12, 28 and 84

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no statistical data available to report.

[2] - 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: For this outcome, Only 1 reporting group was applicable.

End point values	All NEMI			
Subject group type	Reporting group			
Number of subjects analysed	22[3]			
Units: Fold change				
number (not applicable)				
Day 12,222834_s_at, GNG12	1.78			
Day 12,210390_s_at, CCL15	1.72			
Day 12,212294_at, GNG12	1.67			
Day 12,226497_s_at, FLT1	1.57			
Day 12, 204356_at, LIMK1	1.54			
Day 12, 203923_s_at, CYBB	1.51			
Day 12, 219748_at, TREML2	-1.51			
Day 12, 1555086_at, STAT5B	-1.51			
Day 12, 211883_x_at, CEACAM1	-1.51			
Day 12, 224909_s_at, PREX1	-1.51			
Day 12, 239170_at, ACTR3	-1.51			
Day 12, 212550_at, STAT5B	-1.52			
Day 12, 202178_at, PRKCZ	-1.52			
Day 12, 219633_at, TTPAL	-1.53			

Day 12, 204285_s_at, PMAIP1	-1.56			
Day 12, 1555088_x_at, STAT5B	-1.56			
Day 12, 227817_at, PRKCB	-1.57			
Day 12, 205632_s_at, PIP5K1B	-1.58			
Day 12, 202018_s_at, LTF	-1.59			
Day 12, 232763_at, TLN1	-1.59			
Day 12, 202948_at, IL1R1	-1.60			
Day 12, 1569830_at, PTPRC	-1.63			
Day 12, 215561_s_at, IL1R1	-1.69			
Day 12, 228031_at, TTPAL	-1.71			
Day 12, 209498_at, CEACAM1	-1.75			
Day 12, 204563_at, SELL	-1.87			
Day 12, 205118_at, FPR1	-1.93			
Day 12, 236172_at, LTB4R	-1.96			
Day 12, 212372_at, MYH10	-2.12			
Day 28, 244313_at, CR1	1.99			
Day 28, 213093_at, PRKCA	1.53			
Day 28, 205778_at, KLK7	-1.54			
Day 84, 233694_at, HSPA1L	1.88			
Day 84, 208304_at, CCR3	1.83			
Day 84, 215101_s_at, CXCL5	1.82			
Day 84,214974_x_at ,CXCL5	1.80			
Day 84, 207852_at, CXCL5	1.63			
Day 84, 1555759_a_at, CCL5	-1.51			
Day 84, 207535_s_at, NFKB2	-1.53			
Day 84, 234212_at, ACTR2	-1.57			
Day 84, 207794_at, CCR2	-1.58			
Day 84, 206978_at, CCR2	-1.64			
Day 84, 211889_x_at, CEACAM1	-1.69			
Day 84, 206219_s_at, VAV1	-1.71			
Day 84, 209498_at, CEACAM1	-1.72			
Day 84, 206576_s_at, CEACAM1	-1.75			
Day 84, 211883_x_at, CEACAM1	-1.76			

Notes:

[3] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change in mRNA transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in Placebo treatment group

End point title	Change in mRNA transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in Placebo treatment group[4][5]

End point description:

Saline-induced sputum samples were collected at the indicated time-points to determine the alterations in previously identified immune cell mechanisms specifically related to neutrophil function by identifying the changes in mRNA transcriptome in induced sputum. Baseline was defined as screening visit. The log2 transformed mRNA intensities for each probe set were analysed in a separate repeated measures model. Back transformed baseline-adjusted ratios and two-sided unadjusted p-values were calculated for each visit as the specified time-point value/baseline value. These ratios were converted to fold change values; if ratio >= 1 then fold change=ratio or if ratio < 1 then fold change = -1/ratio. Data for

pre-specified probe sets that meet the criteria fold change >1.5 or <-1.5 and p<0.05 for All Placebo group is presented. In the categories column we have included time-point, Probe ID and Gene label.

End point type	Primary

End point timeframe:

Baseline (Screening) and Days 12, 28 and 84

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no statistical data available to report.

[5] - 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: For this outcome, Only 1 reporting group was applicable.

End point values	All Placebo			
Subject group type	Reporting group			
Number of subjects analysed	22[6]			
Units: Fold Change				
number (not applicable)				
Day 12, 222834_s_at, GNG12	2.29			
Day 12, 207852_at, CXCL5	1.81			
Day 12, 212294_at, GNG12	1.79			
Day 12, 209576_at, GNAI1	1.61			
Day 12, 213281_at, JUN	1.51			
Day 12, 222880_at, AKT3	1.51			
Day 12, 205026_at, STAT5B	-1.50			
Day 12, 201783_s_at, RELA	-1.50			
Day 12, 227404_s_at, EGR1	-1.51			
Day 12, 1552552_s_at,CLEC4C	-1.54			
Day 12, 211823_s_at,PXN	-1.55			
Day 12,206978_at,CCR2	-1.55			
Day 12,206219_s_at,VAV1	-1.56			
Day 12,219748_at,TREML2	-1.56			
Day 12,207794_at,CCR2	-1.58			
Day 12,211561_x_at,MAPK14	-1.59			
Day 12,226507_at,PAK1	-1.59			
Day 12,232068_s_at,TLR4	-1.60			
Day 12,209282_at,PRKD2	-1.60			
Day 12,226080_at,SSH2	-1.61			
Day 12,212550_at,STAT5B	-1.64			
Day 12,212372_at,MYH10	-1.64			
Day 12,214022_s_at,IFITM1	-1.66			
Day 12,217484_at,CR1	-1.67			
Day 12,206244_at,CR1	-1.68			
Day 12,1552480_s_at,PTPRC	-1.68			
Day 12,1554114_s_at,SSH2	-1.69			
Day 12,201601_x_at,IFITM1	-1.75			
Day 12,205842_s_at,JAK2	-1.75			
Day 12,228603_at, ACTR3	-1.75			
Day 12,230100_x_at,PAK1	-1.77			
Day 12,239307_at,MYH11	-1.88			
Day 12,223750_s_at,TLR10	-1.88			
Day 12,208488_s_at,CR1	-1.92			

Day 12,204563_at,SELL	-2.70			
Day 28, 222834_s_at,GNG12	1.91			
Day 84,226498_at,FLT1	4.10			
Day 84,216598_s_at,CCL2	1.75			
Day 84,1562439_at,NCOA3	1.52			
Day 84,201087_at,PXN	-1.52			
Day 84,224909_s_at,PREX1	-1.52			
Day 84,211823_s_at,PXN	-1.53			
Day 84,209615_s_at,PAK1	-1.54			
Day 84,211561_x_at,MAPK14	-1.59			
Day 84,203749_s_at,RARA	-1.60			
Day 84,219748_at,TREML2	-1.61			
Day 84,207008_at,CXCR2	-1.66			
Day 84,244313_at,CR1	-1.67			
Day 84,202530_at,MAPK14	-1.69			
Day 84,228648_at,LRG1	-1.71			
Day 84,208488_s_at,CR1	-1.71			
Day 84,228795_at,PRKCB	-1.73			
Day 84,1552480_s_at,PTPRC	-1.76			
Day 84,232068_s_at,TLR4	-1.77			
Day 84,221060_s_at,TLR4	-1.78			
Day 84,201601_x_at,IFITM1	-1.79			
Day 84,202018_s_at,LTF	-1.82			
Day 84,217209_at,CEACAM3	-1.85			
Day 84,214022_s_at,IFITM1	-1.89			
Day 84,217552_x_at,CR1	-1.89			
Day 84,203591_s_at,CSF3R	-1.91			
Day 84,205118_at,FPR1	-1.92			
Day 84,1553297_a_at,CSF3R	-1.96			
Day 84,204563_at,SELL	-2.23			
Day 84,219669_at,CD177	-2.47			

Notes:

[6] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Primary: Change in Messenger Ribonucleic acid (mRNA) transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in All NEMI/All Placebo comparison treatment group

End point title	Change in Messenger Ribonucleic acid (mRNA) transcriptome in induced sputum after 12, 28 and 84 days of treatment (selected probe sets with fold change >1.5 or <-1.5 and p<0.05) in All NEMI/All Placebo comparison treatment group[7]

End point description:

Saline-induced sputum samples were collected at the indicated time-points to determine the alterations in previously identified immune cell mechanisms specifically related to neutrophil function by identifying the changes in mRNA transcriptome in induced sputum. Baseline was defined as screening visit. The log2 transformed mRNA intensities for each probe set were analyzed in a separate repeated measures model. Back transformed baseline-adjusted ratios between All NEMI vs All Placebo and two-sided unadjusted p-values were calculated for each visit as All NEMI/All Placebo. These ratios were converted to fold change values; if ratio >= 1 then fold change=ratio or if ratio < 1 then fold change = -1/ratio. Data for pre-specified probe sets that meet the criteria fold change >1.5 or <-1.5 and p<0.05 for All NEMI/All Placebo comparison is presented. In the categories column we have included time-point, Probe

ID and Gene label.

End point type	Primary

End point timeframe:

Baseline (Screening) and Days 12, 28 and 84

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There is no statistical data available to report.

End point values	All NEMI/All Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	22[8]			
Units: Fold Change				
number (not applicable)				
Day 12,200671_s_at,SPTBN1	-1.74			
Day 12,226342_at,SPTBN1	-1.89			
Day 12,200672_x_at,SPTBN1	-1.60			
Day 12,209576_at,GNAI1	-1.62			
Day 12,202178_at,PRKCZ	-1.55			
Day 28,244313_at,CR1	2.75			
Day 28,223750_s_at,TLR10	2.66			
Day 28,217552_x_at,CR1	2.25			
Day 28,206244_at,CR1	2.01			
Day 28,208488_s_at,CR1	1.95			
Day 28,232068_s_at,TLR4	1.71			
Day 28,1553297_a_at,CSF3R	1.71			
Day 28,1552798_a_at,TLR4	1.68			
Day 28,223943_s_at,GNG2	1.63			
Day 28,221060_s_at,TLR4	1.58			
Day 28,239695_at,JAK1	1.52			
Day 28,234290_x_at,MYH14	-1.52			
Day 28,1568377_x_at,DEFB124	-1.52			
Day 28,1555765_a_at,GNG4	-1.53			
Day 28,201464_x_at,JUN	-1.57			
Day 28,201465_s_at,JUN	-1.68			
Day 28,239381_at,KLK7	-1.69			
Day 28,205778_at,KLK7	-1.71			
Day 28,213281_at,JUN	-1.72			
Day 84,208304_at,CCR3	2.52			
Day 84,1553297_a_at,CSF3R	2.25			
Day 84,203591_s_at,CSF3R	1.98			
Day 84,221060_s_at,TLR4	1.83			
Day 84,202530_at,MAPK14	1.77			
Day 84,244313_at,CR1	1.60			
Day 84,203872_at,ACTA1	1.53			
Day 84,216944_s_at,ITPR1	-1.51			
Day 84,215195_at,PRKCA	-1.66			
Day 84,226498_at,FLT1	-5.18			

Notes:

[8] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Specific Imaging Airway Volume (siVaw) at Functional Residual Capacity (FRC) and Total Lung Capacity (TLC) for Individual Lobes

End point title	Change from Baseline in Specific Imaging Airway Volume (siVaw) at Functional Residual Capacity (FRC) and Total Lung Capacity (TLC) for Individual Lobes

End point description:

siVaw was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Baseline (Screening), Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (n=X1, X2 in the category title). This table presents the untrimmed data (in rows with categories containing untrimmed), SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening), Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[9]	22[10]		
Units: Milliliters per Liter				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 12,n=17,16	1.020 (0.854 to 1.217)	1.038 (0.880 to 1.225)		
FRC,Scan Trimmed,Right Upper,Day 28,n=16,18	1.027 (0.838 to 1.258)	1.030 (0.924 to 1.147)		
FRC,Scan Trimmed,Left Upper,Day 12,n=18,17	0.970 (0.798 to 1.180)	0.993 (0.857 to 1.151)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,19	1.008 (0.779 to 1.304)	1.053 (0.937 to 1.184)		
FRC,Scan Trimmed,Right Middle,Day 12,n=17,16	1.294 (0.904 to 1.852)	1.008 (0.856 to 1.188)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,18	1.071 (0.773 to 1.484)	0.973 (0.865 to 1.093)		
FRC,Scan Trimmed,Right Lower,Day 12,n=17,17	1.025 (0.873 to 1.204)	1.029 (0.858 to 1.236)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,19	1.032 (0.872 to 1.222)	1.042 (0.924 to 1.174)		
FRC,Scan Trimmed,Left Lower,Day 12,n=17,17	1.012 (0.894 to 1.145)	1.032 (0.886 to 1.201)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,19	0.973 (0.862 to 1.097)	1.062 (0.974 to 1.157)		
TLC,Scan Trimmed,Right Upper,Day 12,n=19,17	0.991 (0.908 to 1.080)	0.999 (0.876 to 1.141)		
TLC,Scan Trimmed,Right Upper,Day 28,n=18,19	0.951 (0.870 to 1.040)	0.964 (0.860 to 1.081)		
TLC,Scan Trimmed,Left Upper,Day 12,n=20,18	0.954 (0.897 to 1.014)	0.968 (0.852 to 1.101)		

TLC,Scan Trimmed,Left Upper,Day 28,n=18,20	0.935 (0.860 to 1.017)	0.950 (0.872 to 1.035)		
TLC,Scan Trimmed,Right Middle,Day 12,n=18,17	0.958 (0.835 to 1.099)	1.008 (0.891 to 1.140)		
TLC,Scan Trimmed,Right Middle,Day 28,n=18,19	0.969 (0.837 to 1.122)	0.900 (0.815 to 0.994)		
TLC,Scan Trimmed,Right Lower,Day 12,n=20,18	1.054 (0.936 to 1.187)	0.963 (0.853 to 1.087)		
TLC,Scan Trimmed,Right Lower,Day 28,n=18,20	0.952 (0.848 to 1.068)	0.899 (0.814 to 0.993)		
TLC,Scan Trimmed,Left Lower,Day 12,n=20,18	0.967 (0.911 to 1.026)	1.004 (0.887 to 1.136)		
TLC,Scan Trimmed,Left Lower,Day 28,n=18,20	0.953 (0.852 to 1.066)	0.950 (0.868 to 1.040)		
FRC,Untrimmed,Right Upper,Day 12,n= 17,16	0.900 (0.670 to 1.209)	1.071 (0.851 to 1.349)		
FRC,Untrimmed,Right Upper, Day 28,n=16,18	1.001 (0.720 to 1.390)	1.073 (0.917 to 1.255)		
FRC,Untrimmed,Left Upper, Day 12,n=18,17	1.001 (0.683 to 1.468)	0.956 (0.731 to 1.251)		
Untrimmed,Left Upper, Day 28,n=16,19	1.082 (0.669 to 1.750)	1.065 (0.814 to 1.393)		
FRC,Untrimmed,Right Middle, Day 12,n=17,16	1.347 (0.709 to 2.559)	1.058 (0.825 to 1.356)		
FRC,Untrimmed,Right Middle, Day 28,n=16,18	1.118 (0.696 to 1.797)	1.007 (0.815 to 1.244)		
FRC,Untrimmed,Right Lower, Day 12,n=17,17	1.237 (0.796 to 1.923)	1.014 (0.736 to 1.397)		
FRC,Untrimmed,Right Lower, Day 28,n=16,19	1.241 (0.841 to 1.831)	1.031 (0.816 to 1.302)		
FRC,Untrimmed,Left Lower, Day 12,n=17,17	0.967 (0.754 to 1.239)	1.002 (0.702 to 1.429)		
FRC,Untrimmed,Left Lower, Day 28,n=16,19	0.815 (0.590 to 1.125)	1.142 (0.945 to 1.381)		
TLC,Untrimmed,Right Upper,Day 12,n=19,17	0.982 (0.862 to 1.118)	1.002 (0.831 to 1.209)		
TLC,Untrimmed,Right Upper, Day 28,n=18,19	0.884 (0.776 to 1.006)	0.941 (0.804 to 1.100)		
TLC,Untrimmed,Left Upper, Day 12,n=20,18	0.955 (0.861 to 1.059)	0.942 (0.789 to 1.125)		
TLC,Untrimmed,Left Upper, Day 28,n=18,20	0.949 (0.860 to 1.046)	0.926 (0.813 to 1.055)		
TLC,Untrimmed,Right Middle, Day 12,n=18,17	0.942 (0.777 to 1.142)	0.970 (0.811 to 1.161)		
TLC,Untrimmed,Right Middle, Day 28,n=18,19	0.691 (0.475 to 1.005)	0.892 (0.784 to 1.014)		
TLC,Untrimmed,Right Lower, Day 12,n=20,18	1.131 (0.898 to 1.424)	0.895 (0.745 to 1.075)		
TLC,Untrimmed,Right Lower, Day 28,n=18,20	0.948 (0.791 to 1.135)	0.865 (0.753 to 0.993)		
TLC,Untrimmed,Left Lower, Day 12,n=20,18	0.982 (0.885 to 1.089)	0.989 (0.831 to 1.178)		
TLC,Untrimmed,Left Lower, Day 28,n=18,20	0.894 (0.693 to 1.152)	0.967 (0.858 to 1.090)		

Notes:

[9] - All Subjects Population

[10] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in siVaw at FRC and TLC for Individual Lobes at Day 28

End point title	Change from Baseline (Day 12) in siVaw at FRC and TLC for Individual Lobes at Day 28

End point description:

siVaw is a measure of the volume in an individual's airway corrected for their lobar volume derived from the high resolution computed tomography (HRCT). It was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Baseline (Screening), Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[11]	22[12]		
Units: Milliliters per Liter				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 28,n=16,17	0.998 (0.917 to 1.086)	0.988 (0.909 to 1.074)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,18	0.987 (0.905 to 1.077)	1.014 (0.904 to 1.137)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,17	1.003 (0.876 to 1.149)	0.930 (0.828 to 1.043)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,18	0.938 (0.845 to 1.041)	1.020 (0.884 to 1.176)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,18	0.947 (0.849 to 1.057)	1.042 (0.905 to 1.200)		
TLC, Scan Trimmed,Right Upper,Day 28,n=17,18	0.963 (0.875 to 1.061)	0.965 (0.928 to 1.004)		
TLC, Scan Trimmed,Left Upper,Day 28,n=17,19	0.984 (0.896 to 1.079)	0.999 (0.940 to 1.061)		
TLC, Scan Trimmed,Right Middle,Day 28,n=17,18	0.807 (0.601 to 1.084)	0.897 (0.829 to 0.971)		
TLC, Scan Trimmed,Right Lower,Day 28,n=17,19	0.945 (0.848 to 1.052)	0.943 (0.892 to 0.997)		
TLC, Scan Trimmed,Left Lower,Day 28,n=17,19	0.950 (0.863 to 1.046)	0.963 (0.868 to 1.069)		

Notes:

[11] - All Subjects Population

[12] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in siVaw at FRC and TLC for Individual Regions

End point title	Change from Baseline in siVaw at FRC and TLC for Individual Regions

End point description:

siVaw was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Baseline (Screening), Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (n=X1, X2 in the category title).This table presents the untrimmed data (in rows with categories containing untrimmed), SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening), Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[13]	22[14]		
Units: Milliliters per Liter				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 12,n=18,17	0.996 (0.840 to 1.180)	1.024 (0.888 to 1.181)		
FRC,Scan Trimmed,Upper,Day 28,n=16,19	1.011 (0.814 to 1.257)	1.029 (0.934 to 1.133)		
FRC,Scan Trimmed,Lower,Day 12,n=17,17	1.003 (0.881 to 1.143)	1.039 (0.901 to 1.199)		
FRC,Scan Trimmed,Lower,Day 28,n=16,19	0.991 (0.873 to 1.125)	1.041 (0.942 to 1.150)		
FRC,Scan Trimmed,Central,Day 12,n=18,17	1.027 (0.917 to 1.151)	1.052 (0.998 to 1.108)		
FRC,Scan Trimmed,Central,Day 28,n=16,19	1.048 (0.928 to 1.183)	1.045 (0.996 to 1.096)		
FRC,Scan Trimmed,Distal,Day 12,n=18,17	0.970 (0.859 to 1.096)	1.029 (0.891 to 1.187)		
FRC,Scan Trimmed,Distal,Day 28,n=16,19	0.980 (0.844 to 1.138)	1.037 (0.945 to 1.138)		
FRC,Scan Trimmed,Total,Day 12,n=18,17	1.023 (0.914 to 1.144)	1.046 (0.989 to 1.106)		
FRC,Scan Trimmed,Total,Day 28,n=16,19	1.041 (0.923 to 1.175)	1.042 (0.994 to 1.091)		
TLC, Scan Trimmed,Upper,Day 12,n=20,18	0.963 (0.904 to 1.026)	0.982 (0.870 to 1.109)		
TLC, Scan Trimmed,Upper,Day 28,n=18,20	0.939 (0.863 to 1.022)	0.945 (0.865 to 1.033)		
TLC, Scan Trimmed,Lower,Day 12,n=20,18	0.996 (0.924 to 1.074)	0.982 (0.880 to 1.096)		
TLC, Scan Trimmed,Lower,Day 28,n=18,20	0.958 (0.852 to 1.078)	0.925 (0.848 to 1.009)		
TLC, Scan Trimmed,Central,Day 12,n=20,18	1.011 (0.981 to 1.042)	1.029 (1.000 to 1.058)		
TLC, Scan Trimmed,Central,Day 28,n=18,20	1.013 (0.979 to 1.048)	1.006 (0.984 to 1.028)		

TLC, Scan Trimmed,Distal,Day 12,n=20,18	0.979 (0.917 to 1.045)	0.981 (0.876 to 1.098)		
TLC, Scan Trimmed,Distal,Day 28,n=18,20	0.948 (0.864 to 1.040)	0.934 (0.860 to 1.015)		
TLC, Scan Trimmed,Total,Day 12,n=20,18	1.004 (0.971 to 1.037)	1.020 (0.982 to 1.060)		
TLC, Scan Trimmed,Total,Day 28,n=18,20	1.001 (0.968 to 1.035)	0.990 (0.967 to 1.014)		
FRC,Untrimmed,Upper,Day 12,n= 18,17	0.967 (0.722 to 1.296)	1.050 (0.842 to 1.309)		
FRC,Untrimmed,Upper, Day 28,n=16,19	1.027 (0.699 to 1.507)	1.066 (0.888 to 1.279)		
FRC,Untrimmed,Lower, Day 12,n=17,17	1.055 (0.786 to 1.415)	1.026 (0.781 to 1.346)		
FRC,Untrimmed, Lower, Day 28,n=16,19	0.991 (0.779 to 1.261)	1.077 (0.886 to 1.308)		
FRC,Untrimmed,Central, Day 12,n=18,17	1.035 (0.928 to 1.153)	1.059 (1.008 to 1.113)		
FRC,Untrimmed,Central, Day 28,n=16,19	1.054 (0.935 to 1.188)	1.048 (0.994 to 1.10)		
FRC,Untrimmed,Distal, Day 12,n=18,17	0.926 (0.729 to 1.177)	1.037 (0.820 to 1.313)		
FRC,Untrimmed,Distal, Day 28,n=16,19	0.981 (0.752 to 1.279)	1.071 (0.892 to 1.285)		
FRC,Untrimmed,Total, Day 12,n=18,17	1.025 (0.913 to 1.151)	1.050 (0.983 to 1.122)		
FRC,Untrimmed,Total, Day 28,n=16,19	1.045 (0.913 to 1.195)	1.046 (0.988 to 1.107)		
TLC,Untrimmed,Upper,Day 12,n= 20,18	0.961 (0.853 to 1.082)	0.959 (0.807 to 1.139)		
TLC,Untrimmed,Upper, Day 28,n=18,20	0.906 (0.818 to 1.003)	0.923 (0.815 to 1.045)		
TLC,Untrimmed,Lower, Day 12,n=20,18	1.035 (0.907 to 1.182)	0.938 (0.804 to 1.095)		
TLC,Untrimmed, Lower, Day 28,n=18,20	0.933 (0.766 to 1.138)	0.916 (0.820 to 1.022)		
TLC,Untrimmed,Central, Day 12,n=20,18	1.012 (0.985 to 1.040)	1.027 (0.998 to 1.057)		
TLC,Untrimmed,Central, Day 28,n=18,20	1.010 (0.974 to 1.047)	1.002 (0.979 to 1.026)		
TLC,Untrimmed,Distal, Day 12,n=20,18	0.996 (0.882 to 1.124)	0.946 (0.807 to 1.110)		
TLC,Untrimmed,Distal, Day 28,n=18,20	0.922 (0.803 to 1.057)	0.918 (0.824 to 1.022)		
TLC,Untrimmed,Total, Day 12,n=20,18	1.000 (0.970 to 1.031)	1.009 (0.962 to 1.059)		
TLC,Untrimmed,Total, Day 28,n=18,20	0.993 (0.950 to 1.038)	0.982 (0.957 to 1.008)		

Notes:

[13] - All Subjects Population

[14] - All Subjects Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Imaging Airway Volume (iVaw) at FRC and TLC for Individual Lobes

End point title	Change from Baseline in Imaging Airway Volume (iVaw) at FRC and TLC for Individual Lobes

End point description:

iVaw was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Screening, Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (n=X1, X2 in the category title). This table presents the untrimmed data (in rows with categories containing untrimmed), SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[15]	22[16]		
Units: Milliliters				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 12,n=18,17	1.007 (0.847 to 1.197)	1.044 (0.879 to 1.240)		
FRC,Scan Trimmed,Right Upper,Day 28,n=16,19	1.016 (0.826 to 1.249)	1.037 (0.931 to 1.155)		
FRC,Scan Trimmed,Left Upper,Day 12,n=18,17	0.965 (0.783 to 1.190)	0.987 (0.830 to 1.173)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,19	0.998 (0.767 to 1.299)	1.062 (0.919 to 1.227)		
FRC,Right Middle,Day 12,n=18,17	1.129 (0.803 to 1.588)	1.014 (0.874 to 1.176)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,19	0.950 (0.739 to 1.221)	1.018 (0.881 to 1.176)		
FRC,Right Lower,Day 12,n=17,17	1.046 (0.884 to 1.237)	1.005 (0.824 to 1.225)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,19	1.042 (0.879 to 1.235)	1.025 (0.889 to 1.181)		
FRC,Left Lower,Day 12,n=17,17	1.003 (0.855 to 1.178)	1.010 (0.832 to 1.226)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,19	0.971 (0.836 to 1.127)	1.029 (0.920 to 1.151)		
TLC,Scan Trimmed,Right Upper,Day 12,n=20,18	0.976 (0.903 to 1.054)	0.982 (0.864 to 1.117)		
TLC,Scan Trimmed,Right Upper,Day 28,n=18,20	0.941 (0.858 to 1.032)	0.946 (0.849 to 1.054)		
TLC,Scan Trimmed,Left Upper,Day 12,n=20,18	0.957 (0.897 to 1.020)	0.958 (0.840 to 1.093)		
TLC,Scan Trimmed,Left Upper,Day 28,n=18,20	0.928 (0.849 to 1.015)	0.938 (0.857 to 1.025)		
TLC,Scan Trimmed,Right Middle,Day 12,n=19,18	0.882 (0.810 to 0.961)	0.988 (0.881 to 1.108)		
TLC,Scan Trimmed,Right Middle,Day 28,n=18,20	0.873 (0.742 to 1.027)	0.895 (0.811 to 0.987)		
TLC,Scan Trimmed,Right Lower,Day 12,n=20,18	1.083 (0.966 to 1.214)	0.937 (0.828 to 1.061)		
TLC,Scan Trimmed,Right Lower,Day 28,n=18,20	0.967 (0.860 to 1.088)	0.877 (0.782 to 0.983)		

TLC,Scan Trimmed,Left Lower,Day 12,n=20,18	0.981 (0.922 to 1.044)	0.981 (0.850 to 1.131)		
TLC,Scan Trimmed,Left Lower,Day 28,n=18,20	0.939 (0.832 to 1.060)	0.923 (0.843 to 1.010)		
FRC,Untrimmed,Right Upper,Day 12,n= 18,17	0.886 (0.652 to 1.203)	1.095 (0.858 to 1.396)		
FRC,Untrimmed,Right Upper, Day 28,n=16,19	0.990 (0.703 to 1.393)	1.083 (0.923 to 1.272)		
FRC,Untrimmed,Left Upper, Day 12,n=18,17	0.996 (0.668 to 1.485)	0.950 (0.696 to 1.297)		
FRC,Untrimmed,Left Upper, Day 28,n=16,19	1.071 (0.656 to 1.749)	1.074 (0.798 to 1.444)		
FRC,Untrimmed,Right Middle, Day 12,n=18,17	1.167 (0.633 to 2.149)	1.157 (0.840 to 1.595)		
FRC,Untrimmed,Right Middle, Day 28,n=16,19	0.991 (0.629 to 1.562)	1.155 (0.819 to 1.631)		
FRC,Untrimmed,Right Lower, Day 12,n=17,17	1.262 (0.791 to 2.015)	0.990 (0.703 to 1.392)		
FRC,Untrimmed,Right Lower, Day 28,n=16,19	1.253 (0.832 to 1.885)	1.014 (0.784 to 1.311)		
FRC,Untrimmed,Left Lower, Day 12,n=17,17	0.959 (0.714 to 1.287)	0.981 (0.655 to 1.469)		
FRC,Untrimmed,Left Lower, Day 28,n=16,19	0.813 (0.571 to 1.157)	1.107 (0.882 to 1.389)		
TLC,Untrimmed,Right Upper,Day 12,n=20,18	0.960 (0.839 to 1.098)	0.984 (0.822 to 1.178)		
TLC,Untrimmed,Right Upper, Day 28,n=18,20	0.874 (0.754 to 1.012)	0.923 (0.797 to 1.069)		
TLC,Untrimmed,Left Upper, Day 12,n=20,18	0.958 (0.853 to 1.075)	0.932 (0.779 to 1.116)		
TLC,Untrimmed,Left Upper, Day 28,n=18,20	0.942 (0.850 to 1.043)	0.914 (0.800 to 1.045)		
TLC,Untrimmed,Right Middle, Day 12,n=19,18	0.872 (0.724 to 1.050)	0.952 (0.806 to 1.124)		
TLC,Untrimmed,Right Middle, Day 28,n=18,20	0.622 (0.367 to 1.053)	0.886 (0.780 to 1.007)		
TLC,Untrimmed,Right Lower, Day 12,n=20,18	1.162 (0.914 to 1.476)	0.871 (0.721 to 1.053)		
TLC,Untrimmed,Right Lower, Day 28,n=18,20	0.963 (0.795 to 1.166)	0.843 (0.725 to 0.981)		
TLC,Untrimmed,Left Lower, Day 12,n=20,18	0.996 (0.888 to 1.117)	0.967 (0.797 to 1.172)		
TLC,Untrimmed,Left Lower, Day 28,n=18,20	0.881 (0.675 to 1.149)	0.940 (0.828 to 1.066)		

Notes:

[15] - All Subjects Population.

[16] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in iVaw at FRC and TLC for Individual Lobes at Day 28

End point title	Change from Baseline (Day 12) in iVaw at FRC and TLC for Individual Lobes at Day 28

End point description:

iVaw is a measure of the volume in an individual's airway derived from the HRCT. It was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Screening, Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left

lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[17]	22[18]		
Units: Milliliters				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 28,n=16,18	0.995 (0.918 to 1.078)	0.977 (0.880 to 1.084)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,18	0.973 (0.891 to 1.063)	1.016 (0.898 to 1.151)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,18	0.958 (0.842 to 1.090)	0.943 (0.838 to 1.061)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,18	0.918 (0.821 to 1.025)	1.008 (0.855 to 1.188)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,18	0.943 (0.852 to 1.045)	1.024 (0.877 to 1.196)		
TLC,Scan Trimmed,Right Upper,Day 28,n=17,19	0.963 (0.875 to 1.060)	0.966 (0.936 to 0.997)		
TLC,Scan Trimmed,Left Upper,Day 28,n=17,19	0.976 (0.885 to 1.076)	0.996 (0.942 to 1.052)		
TLC,Right Middle,Day 28,n=17,19	0.784 (0.571 to 1.077)	0.904 (0.841 to 0.971)		
TLC,Scan Trimmed,Right Lower,Day 28,n=17,19	0.926 (0.826 to 1.038)	0.935 (0.876 to 0.997)		
TLC,Scan Trimmed,Left Lower,Day 28,n=17,19	0.928 (0.833 to 1.035)	0.951 (0.855 to 1.057)		

Notes:

[17] - All Subjects Population.

[18] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in iVaw at FRC and TLC for Individual Regions

End point title	Change from Baseline in iVaw at FRC and TLC for Individual Regions

End point description:

iVaw was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Screening, Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (n=X1, X2 in the category title). This table presents the untrimmed data (in rows with categories containing untrimmed), SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan

trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[19]	22[20]		
Units: Milliliters				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 12,n=18,17	0.987 (0.827 to 1.178)	1.021 (0.869 to 1.200)		
FRC,Scan Trimmed,Upper,Day 28,n=16,19	0.999 (0.800 to 1.246)	1.039 (0.927 to 1.166)		
FRC,Scan Trimmed,Lower,Day 12,n=17,17	1.009 (0.864 to 1.178)	1.017 (0.863 to 1.199)		
FRC,Scan Trimmed,Lower,Day 28,n=16,19	0.993 (0.862 to 1.142)	1.018 (0.899 to 1.152)		
FRC,Scan Trimmed,Central,Day 12,n=18,17	1.025 (0.925 to 1.136)	1.040 (0.985 to 1.097)		
FRC,Scan Trimmed,Central,Day 28,n=16,19	1.040 (0.936 to 1.155)	1.040 (0.974 to 1.110)		
FRC,Scan Trimmed,Distal,Day 12,n=18,17	0.969 (0.847 to 1.107)	1.017 (0.866 to 1.194)		
FRC,Scan Trimmed,Distal,Day 28,n=16,19	0.973 (0.834 to 1.135)	1.032 (0.921 to 1.157)		
FRC,Scan Trimmed,Total,Day 12,n=18,17	1.021 (0.920 to 1.132)	1.034 (0.970 to 1.101)		
FRC,Scan Trimmed,Total,Day 28,n=16,19	1.034 (0.927 to 1.153)	1.037 (0.970 to 1.108)		
TLC,Scan Trimmed,Upper,Day 12,n=20,18	0.959 (0.899 to 1.023)	0.973 (0.860 to 1.101)		
TLC,Scan Trimmed,Upper,Day 28,n=18,20	0.930 (0.851 to 1.015)	0.935 (0.853 to 1.024)		
TLC,Scan Trimmed,Lower,Day 12,n=20,18	1.017 (0.945 to 1.094)	0.960 (0.858 to 1.074)		
TLC,Scan Trimmed,Lower,Day 28,n=18,20	0.958 (0.846 to 1.084)	0.902 (0.823 to 0.989)		
TLC,Scan Trimmed,Central,Day 12,n=20,18	1.019 (0.998 to 1.040)	1.013 (0.988 to 1.040)		
TLC,Scan Trimmed,Central,Day 28,n=18,20	1.006 (0.984 to 1.028)	0.989 (0.965 to 1.013)		
TLC,Scan Trimmed,Distal,Day 12,n=20,18	0.986 (0.924 to 1.053)	0.966 (0.862 to 1.083)		
TLC,Scan Trimmed,Distal,Day 28,n=18,20	0.941 (0.854 to 1.038)	0.918 (0.842 to 1.002)		
TLC,Scan Trimmed,Total,Day 12,n=20,18	1.011 (0.985 to 1.038)	1.005 (0.968 to 1.043)		
TLC,Scan Trimmed,Total,Day 28,n=18,20	0.994 (0.967 to 1.022)	0.973 (0.947 to 1.000)		
FRC,Untrimmed,Upper,Day 12,n= 18,17	0.959 (0.704 to 1.305)	1.047 (0.815 to 1.345)		
FRC,Untrimmed,Upper, Day 28,n=16,19	1.014 (0.685 to 1.499)	1.076 (0.876 to 1.323)		

FRC,Untrimmed,Lower, Day 12,n=17,17	1.060 (0.761 to 1.478)	1.004 (0.741 to 1.359)		
FRC,Untrimmed, Lower, Day 28,n=16,19	0.993 (0.750 to 1.315)	1.052 (0.840 to 1.319)		
FRC,Untrimmed,Central, Day 12,n=18,17	1.033 (0.920 to 1.160)	1.047 (0.967 to 1.134)		
FRC,Untrimmed,Central, Day 28,n=16,19	1.046 (0.926 to 1.182)	1.043 (0.961 to 1.133)		
FRC,Untrimmed,Distal, Day 12,n=18,17	0.924 (0.709 to 1.205)	1.025 (0.788 to 1.333)		
FRC,Untrimmed,Distal, Day 28,n=16,19	0.974 (0.735 to 1.290)	1.066 (0.865 to 1.313)		
FRC,Untrimmed,Total, Day 12,n=18,17	1.023 (0.900 to 1.163)	1.038 (0.941 to 1.145)		
FRC,Untrimmed,Total, Day 28,n=16,19	1.037 (0.898 to 1.198)	1.041 (0.953 to 1.137)		
TLC,Untrimmed,Upper,Day 12,n= 20,18	0.957 (0.841 to 1.089)	0.950 (0.800 to 1.129)		
TLC,Untrimmed,Upper, Day 28,n=18,20	0.897 (0.805 to 0.998)	0.912 (0.804 to 1.035)		
TLC,Untrimmed,Lower, Day 12,n=20,18	1.057 (0.915 to 1.220)	0.917 (0.783 to 1.074)		
TLC,Untrimmed, Lower, Day 28,n=18,20	0.933 (0.759 to 1.147)	0.893 (0.795 to 1.002)		
TLC,Untrimmed,Central, Day 12,n=20,18	1.020 (0.997 to 1.043)	1.012 (0.984 to 1.041)		
TLC,Untrimmed,Central, Day 28,n=18,20	1.003 (0.976 to 1.032)	0.985 (0.959 to 1.012)		
TLC,Untrimmed,Distal, Day 12,n=20,18	1.003 (0.881 to 1.143)	0.932 (0.795 to 1.093)		
TLC,Untrimmed,Distal, Day 28,n=18,20	0.916 (0.793 to 1.056)	0.902 (0.808 to 1.008)		
TLC,Untrimmed,Total, Day 12,n=20,18	1.008 (0.976 to 1.040)	0.994 (0.949 to 1.042)		
TLC,Untrimmed,Total, Day 28,n=18,20	0.986 (0.945 to 1.030)	0.965 (0.936 to 0.995)		

Notes:

[19] - All Subjects Population.

[20] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Imaging Airway Resistance (iRaw) at FRC and TLC for Individual Lobes

End point title	Change from Baseline in Imaging Airway Resistance (iRaw) at FRC and TLC for Individual Lobes

End point description:

iRaw is a measure of the resistance in an individual's airway derived from HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[21]	22[22]		
Units: Kilopascal* seconds per liter (kPa*s/L)				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 12,n=18,17	1.129 (0.641 to 1.991)	0.876 (0.477 to 1.606)		
FRC,Scan Trimmed,Right Upper,Day 28,n=16,19	1.213 (0.569 to 2.586)	0.884 (0.582 to 1.343)		
FRC,Scan Trimmed,Left Upper,Day 12,n=18,17	1.058 (0.631 to 1.774)	0.951 (0.592 to 1.530)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,19	1.151 (0.582 to 2.273)	0.681 (0.438 to 1.060)		
FRC,Scan Trimmed,Right Middle,Day 12,n=18,17	0.559 (0.198 to 1.576)	0.970 (0.578 to 1.627)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,19	1.420 (0.573 to 3.518)	1.275 (0.732 to 2.219)		
FRC,Scan Trimmed,Right Lower,Day 12,n=17,17	0.903 (0.352 to 2.314)	1.149 (0.714 to 1.849)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,19	0.681 (0.251 to 1.850)	0.935 (0.512 to 1.706)		
FRC,Scan Trimmed,Left Lower,Day 12,n=17,17	1.084 (0.642 to 1.832)	0.902 (0.378 to 2.157)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,19	1.576 (0.656 to 3.785)	0.904 (0.642 to 1.274)		
TLC,Scan Trimmed,Right Upper,Day 12,n=20,18	1.058 (0.820 to 1.366)	1.057 (0.739 to 1.511)		
TLC,Scan Trimmed,Right Upper,Day 28,n=18,20	1.307 (0.994 to 1.718)	1.292 (0.951 to 1.755)		
TLC,Scan Trimmed,Left Upper,Day 12,n=20,18	1.129 (0.938 to 1.360)	1.075 (0.662 to 1.747)		
TLC,Scan Trimmed,Left Upper,Day 28,n=18,20	1.212 (0.957 to 1.534)	1.160 (0.851 to 1.580)		
TLC,Scan Trimmed,Right Middle,Day 12,n=19,18	1.190 (0.823 to 1.720)	1.148 (0.747 to 1.763)		
TLC,Scan Trimmed,Right Middle,Day 28,n=18,20	1.749 (0.981 to 3.117)	1.583 (1.002 to 2.502)		
TLC,Scan Trimmed,Right Lower,Day 12,n=20,18	0.727 (0.484 to 1.092)	1.325 (0.860 to 2.041)		
TLC,Scan Trimmed,Right Lower,Day 28,n=18,20	1.143 (0.797 to 1.639)	1.463 (1.077 to 1.988)		
TLC,Scan Trimmed,Left Lower,Day 12,n=20,18	1.003 (0.798 to 1.260)	1.144 (0.714 to 1.833)		
TLC,Scan Trimmed,Left Lower,Day 28,n=18,20	1.259 (0.741 to 2.140)	1.213 (0.907 to 1.623)		

Notes:

[21] - All Subjects Population.

[22] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in iRaw at FRC and TLC for Individual Regions

End point title	Change from Baseline in iRaw at FRC and TLC for Individual Regions

End point description:

iRaw is a measure of the resistance in an individual's airway derived from HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (n=X1, X2 in the category title). This table presents the SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[23]	22[24]		
Units: kPa*s/L				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 12,n=18,17	0.827 (0.448 to 1.526)	0.831 (0.520 to 1.326)		
FRC,Scan Trimmed,Upper,Day 28,n=16,19	1.395 (0.682 to 2.851)	0.776 (0.526 to 1.144)		
FRC,Scan Trimmed,Lower,Day 12,n=17,17	1.112 (0.553 to 2.236)	1.066 (0.510 to 2.225)		
FRC,Scan Trimmed,Lower,Day 28,n=16,19	1.071 (0.515 to 2.230)	0.912 (0.598 to 1.391)		
FRC,Scan Trimmed,Central,Day 12,n=18,17	0.932 (0.637 to 1.364)	0.888 (0.729 to 1.082)		
FRC,Scan Trimmed,Central,Day 28,n=16,19	0.876 (0.606 to 1.266)	0.871 (0.694 to 1.094)		
FRC,Scan Trimmed,Distal,Day 12,n=18,17	1.001 (0.625 to 1.602)	1.098 (0.563 to 2.144)		
FRC,Scan Trimmed,Distal,Day 28,n=16,19	1.169 (0.559 to 2.443)	0.857 (0.589 to 1.247)		
FRC,Scan Trimmed,Total,Day 12,n=18,17	0.985 (0.673 to 1.441)	0.972 (0.711 to 1.329)		
FRC,Scan Trimmed,Total,Day 28,n=16,19	1.045 (0.656 to 1.665)	0.913 (0.701 to 1.190)		
TLC,Scan Trimmed,Upper,Day 12,n=20,18	1.142 (0.888 to 1.469)	1.167 (0.727 to 1.872)		
TLC,Scan Trimmed,Upper,Day 28,n=18,20	1.540 (1.106 to 2.145)	1.271 (0.956 to 1.690)		
TLC,Scan Trimmed,Lower,Day 12,n=20,18	0.860 (0.649 to 1.141)	1.206 (0.835 to 1.741)		
TLC,Scan Trimmed,Lower,Day 28,n=18,20	1.142 (0.734 to 1.775)	1.315 (1.004 to 1.723)		
TLC,Scan Trimmed,Central,Day 12,n=20,18	0.987 (0.876 to 1.111)	1.005 (0.882 to 1.146)		

TLC,Scan Trimmed,Central,Day 28,n=18,20	0.985 (0.914 to 1.061)	1.057 (0.943 to 1.186)		
TLC,Scan Trimmed,Distal,Day 12,n=20,18	0.959 (0.726 to 1.268)	1.278 (0.824 to 1.983)		
TLC,Scan Trimmed,Distal,Day 28,n=18,20	1.332 (0.869 to 2.040)	1.288 (0.993 to 1.669)		
TLC,Scan Trimmed,Total,Day 12,n=20,18	0.993 (0.831 to 1.187)	1.109 (0.853 to 1.443)		
TLC,Scan Trimmed,Total,Day 28,n=18,20	1.196 (0.959 to 1.492)	1.202 (0.990 to 1.460)		

Notes:

[23] - All Subjects Population.

[24] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Lobes

End point title	Change from Baseline in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Lobes

End point description:

siRaw is a measure of the resistance in an individual's airway corrected for their lobar volume derived from the HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analysed (represented by n=X1, X2 in the category title). This table presents the SCRD12 scan trim pair data (in rows with categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[25]	22[26]		
Units: kPa*s				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 12,n=17,16	1.117 (0.627 to 1.989)	0.961 (0.539 to 1.711)		
FRC,Scan Trimmed,Right Upper,Day 28,n=16,18	1.200 (0.574 to 2.510)	0.923 (0.599 to 1.424)		
FRC,Scan Trimmed,Left Upper,Day 12,n=18,17	1.053 (0.642 to 1.726)	0.945 (0.604 to 1.479)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,19	1.139 (0.586 to 2.215)	0.687 (0.457 to 1.032)		
FRC,Scan Trimmed,Right Middle,Day 12,n=17,16	0.496 (0.163 to 1.511)	1.022 (0.593 to 1.761)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,18	1.259 (0.521 to 3.043)	1.424 (0.836 to 2.424)		

FRC,Scan Trimmed,Right Lower,Day 12,n=17,17	0.921 (0.362 to 2.342)	1.121 (0.715 to 1.758)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,19	0.688 (0.257 to 1.840)	0.920 (0.521 to 1.624)		
FRC,Scan Trimmed,Left Lower,Day 12,n=17,17	1.075 (0.648 to 1.785)	0.884 (0.386 to 2.021)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,19	1.573 (0.669 to 3.701)	0.876 (0.634 to 1.212)		
TLC,Scan Trimmed,Right Upper,Day 12,n=19,17	1.037 (0.788 to 1.364)	1.035 (0.711 to 1.509)		
TLC,Scan Trimmed,Right Upper,Day 28,n=18,19	1.292 (0.992 to 1.684)	1.262 (0.912 to 1.747)		
TLC,Scan Trimmed,Left Upper,Day 12,n=20,18	1.133 (0.946 to 1.358)	1.064 (0.659 to 1.720)		
TLC,Scan Trimmed,Left Upper,Day 28,n=18,20	1.203 (0.955 to 1.515)	1.145 (0.843 to 1.554)		
TLC,Scan Trimmed,Right Middle,Day 12,n=18,17	1.094 (0.730 to 1.639)	1.101 (0.690 to 1.758)		
TLC,Scan Trimmed,Right Middle,Day 28,n=18,19	1.575 (0.965 to 2.570)	1.557 (0.955 to 2.538)		
TLC,Scan Trimmed,Right Lower,Day 12,n=20,18	0.747 (0.498 to 1.120)	1.290 (0.842 to 1.976)		
TLC,Scan Trimmed,Right Lower,Day 28,n=18,20	1.161 (0.814 to 1.654)	1.427 (1.065 to 1.912)		
TLC,Scan Trimmed,Left Lower,Day 12,n=20,18	1.018 (0.810 to 1.278)	1.118 (0.715 to 1.747)		
TLC,Scan Trimmed,Left Lower,Day 28,n=18,20	1.240 (0.735 to 2.092)	1.178 (0.876 to 1.584)		

Notes:

[25] - All Subjects Population.

[26] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lung Lobar Volume (iVlobe) at FRC and TLC for Individual Lobes

End point title	Change from Baseline in lung Lobar Volume (iVlobe) at FRC and TLC for Individual Lobes

End point description:

Change from Baseline in lung lobar volumes was measured at FRC and TLC scan conditions. Data was collected at longitudinal time points: Baseline (Screening), Day 12 and Day 28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe). The value at Screening was considered as Baseline. Change from baseline is the post-Baseline value minus the Baseline value. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI.There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Liters				
geometric mean (confidence interval 95%)				
FRC,Right Upper,Day 12,n=17,16	0.989 (0.921 to 1.063)	0.971 (0.935 to 1.009)		
FRC,Right Upper,Day 28,n=16,18	0.989 (0.929 to 1.053)	0.999 (0.952 to 1.048)		
FRC,Left Upper,Day 12,n=18,17	0.995 (0.938 to 1.056)	0.993 (0.924 to 1.068)		
FRC,Left Upper,Day 28,n=16,19	0.990 (0.935 to 1.048)	1.008 (0.955 to 1.064)		
FRC,Right Middle,Day 12,n=17,16	0.931 (0.819 to 1.057)	0.979 (0.949 to 1.010)		
FRC,Right Middle,Day 28,n=16,18	0.887 (0.708 to 1.111)	1.010 (0.964 to 1.060)		
FRC,Right Lower,Day 12,n=18,17	1.021 (0.928 to 1.123)	0.976 (0.908 to 1.048)		
FRC,Right Lower,Day 28,n=16,19	1.009 (0.907 to 1.124)	0.984 (0.927 to 1.044)		
FRC,Left Lower,Day 12,n=18,17	0.996 (0.917 to 1.082)	0.979 (0.905 to 1.059)		
FRC,Left Lower,Day 28,n=16,19	0.998 (0.915 to 1.089)	0.969 (0.898 to 1.045)		
TLC,Right Upper,Day 12,n=19,17	0.991 (0.964 to 1.020)	0.992 (0.976 to 1.007)		
TLC,Right Upper,Day 28,n=18,19	0.989 (0.967 to 1.012)	0.984 (0.965 to 1.004)		
TLC,Left Upper,Day 12,n=20,18	1.003 (0.985 to 1.022)	0.990 (0.975 to 1.005)		
TLC,Left Upper,Day 28,n=18,20	0.992 (0.978 to 1.008)	0.987 (0.968 to 1.006)		
TLC,Right Middle,Day 12,n=19,17	0.935 (0.815 to 1.072)	0.990 (0.960 to 1.022)		
TLC,Right Middle,Day 28,n=18,19	0.900 (0.741 to 1.094)	0.998 (0.969 to 1.028)		
TLC,Right Lower,Day 12,n=20,18	1.027 (0.981 to 1.076)	0.973 (0.950 to 0.997)		
TLC,Right Lower,Day 28,n=18,20	1.016 (0.963 to 1.072)	0.975 (0.946 to 1.005)		
TLC,Left Lower,Day 12,n=20,18	1.015 (0.982 to 1.048)	0.977 (0.937 to 1.019)		
TLC,Left Lower,Day 28,n=18,20	0.985 (0.953 to 1.018)	0.971 (0.929 to 1.015)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in lung Lobar Volume (iVlobe) at FRC and TLC for Individual Regions

End point title	Change from Baseline in lung Lobar Volume (iVlobe) at FRC and TLC for Individual Regions

End point description:

Change from Baseline in lung lobar volumes was measured at FRC and TLC scan conditions. Data was collected at longitudinal time points: Baseline (Screening), Day 12 and Day 28. At each time point it was measure at 5 Regions (Upper, Lower, Central, Distal & Total). The value at Screening was considered as Baseline. Change from Baseline is the post-Baseline value minus the Baseline value. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI.There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Liters				
geometric mean (confidence interval 95%)				
FRC,Upper,Day 12,n=18,17	0.991 (0.935 to 1.051)	0.997 (0.932 to 1.068)		
FRC,Upper,Day 28,n=16,19	0.987 (0.932 to 1.045)	1.010 (0.961 to 1.061)		
FRC,Lower,Day 12,n=18,17	1.008 (0.923 to 1.100)	0.979 (0.911 to 1.051)		
FRC,Lower,Day 28,n=16,19	1.002 (0.912 to 1.101)	0.978 (0.918 to 1.041)		
FRC,Total,Day 12,n=18,17	0.998 (0.931 to 1.070)	0.988 (0.925 to 1.056)		
FRC,Total,Day 28,n=16,19	0.993 (0.925 to 1.065)	0.995 (0.944 to 1.049)		
TLC,Upper,Day 12,n=20,18	0.997 (0.980 to 1.013)	0.991 (0.978 to 1.004)		
TLC,Upper,Day 28,n=18,20	0.990 (0.978 to 1.002)	0.989 (0.972 to 1.006)		
TLC,Lower,Day 12,n=20,18	1.021 (0.985 to 1.057)	0.977 (0.954 to 1.001)		
TLC,Lower,Day 28,n=18,20	1.000 (0.961 to 1.040)	0.975 (0.947 to 1.004)		
TLC,Total,Day 12,n=20,18	1.008 (0.985 to 1.030)	0.985 (0.970 to 1.000)		
TLC,Total,Day 28,n=18,20	0.993 (0.972 to 1.015)	0.983 (0.962 to 1.004)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Trachea length and diameter at FRC and TLC

End point title	Change from Baseline in Trachea length and diameter at FRC and TLC

End point description:

Trachea length and diameter was derived from HRCT. It was measured at both FRC and TLC scan conditions. The value at Screening was considered as Baseline. Change from Baseline is the post-Baseline value minus the Baseline value. The change from Baseline data is presented for Day 12 and Day 28 for trachea length and diameter. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI.There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[27]	22[28]		
Units: Millimeters				
arithmetic mean (standard deviation)				
FRC,Length,Day 12,n=18,17	0.094 (± 7.2507)	0.972 (± 6.5552)		
FRC,Length,Day 28,n=16,19	0.796 (± 7.7795)	0.281 (± 5.1808)		
FRC,Diameter,Day 12,n=18,17	0.225 (± 1.3641)	0.252 (± 1.0023)		
FRC,Diameter,Day 28,n=16,19	0.225 (± 1.3812)	0.116 (± 1.1600)		
TLC,Length,Day 12,n=20,18	-0.164 (± 2.8331)	0.827 (± 3.1842)		
TLC,Length,Day 28,n=18,20	-0.094 (± 2.8480)	0.069 (± 3.4882)		
TLC,Diameter,Day 12,n=20,18	0.134 (± 0.4670)	0.070 (± 0.4222)		
TLC,Diameter,Day 28,n=18,20	0.076 (± 0.4751)	-0.188 (± 0.4983)		

Notes:

[27] - All Subjects Population.

[28] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Peak Expiratory Flow (PEF)

End point title	Peak Expiratory Flow (PEF)

End point description:

PEF measurements were taken (in triplicate) daily in the morning before dose administration, as soon as it is safe for the participant to do so. The best/highest result was recorded. Participants were provided with a handheld device. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI. There was no intent to compare two devices. Data for this outcome was not available as there was no value added to produce PEF tables for 84 days of PEF data.

End point type	Secondary

End point timeframe:

Up to Day 84

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[29]	0[30]		
Units: Liters per minute				
arithmetic mean (standard deviation)	()	()		

Notes:

[29] - All Subjects Population.

[30] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean number of occasions of Rescue usage per day

End point title	Mean number of occasions of Rescue usage per day

End point description:

For reliever/rescue use, bronchodilator use recorded in the diary was summarized as the mean number of occasions of rescue use per day.where a rescue-free day was defined as a 24-hour period in which the number of occasions of bronchodilator use was zero. Number of occasions bronchodilator taken in the last 24 hours were collected in the daily diary. The mean number of occasions of rescue use per day, were calculated for each participant during the four weekly periods (Weeks 1 to 4; Weeks 5-8 and Weeks 9-12). The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI.There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Weeks 1 to 4; Weeks 5 to 8 and Weeks 9 to 12

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[31]	22[32]		
Units: Rescue use per day				
arithmetic mean (standard deviation)				
Weeks 1-4,n=22,21	3.05 (± 2.520)	2.77 (± 2.432)		
Weeks 5-8,n=19,20	2.93 (± 2.342)	2.81 (± 2.827)		
Weeks 9-12,n=19,20	3.19 (± 2.065)	2.84 (± 2.569)		

Notes:

[31] - All Subjects Population.

[32] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Rescue Medication Free Days

End point title	Mean Rescue Medication Free Days

End point description:

For reliever/rescue use, bronchodilator use recorded in the diary was summarized as the mean number of occasions of rescue use per day, where a rescue-free day was defined as a 24-hour period in which the number of occasions of bronchodilator use was zero. Number of occasions bronchodilator taken in the last 24 hours were collected in the daily diary. The mean number of rescue free days were calculated for each participant during the four weekly periods (Weeks 1 to 4; Weeks 5-8 and Weeks 9-12). The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI. There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Weeks 1 to 4; Weeks 5 to 8 and Weeks 9 to 12

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[33]	22[34]		
Units: Days				
arithmetic mean (standard deviation)				
Weeks 1-4,n=22,21	7.5 (± 9.21)	7.7 (± 10.06)		
Weeks 5-8,n=19,20	5.8 (± 8.58)	9.0 (± 12.14)		
Weeks 9-12,n=19,20	3.7 (± 6.68)	7.9 (± 11.14)		

Notes:

[33] - All Subjects Population.

[34] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Forced Expiratory Volume in One Second (FEV1) and Forced Vital Capacity (FVC)

End point title	Change from Baseline in Forced Expiratory Volume in One Second (FEV1) and Forced Vital Capacity (FVC)

End point description:

FEV1 is the volume of air that can forcibly be blown out in one second. A triplicate FEV1 measurement were taken daily in the morning before dose administration using the site’s spirometer as soon as it was safe to do so. FVC is defined as the amount of air that can be forcibly exhaled from the lungs after taking the deepest breath possible. Baseline is the latest available measurement from Day 2 Within 48 hours /discharge (On Treatment) and Day 1 (Pre-Treatment). Change from Baseline is the post-Baseline value minus Baseline value. The study had a protocol amendment to reflect changes in manufacturing device from DISKUS to ELLIPTA after study had been initiated, but the 2 treatment arms remained the same i.e. Placebo and NEMI.There was no intent to compare two devices. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title).

End point type	Secondary

End point timeframe:

Baseline and Days 12, 28, 56, 84

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[35]	22[36]		
Units: Liters				
arithmetic mean (standard deviation)				
FEV1,Day 12,n=20,18	-0.001 (± 0.1681)	0.084 (± 0.1879)		
FEV1,Day 28,n=19,20	0.005 (± 0.2227)	0.094 (± 0.2035)		
FEV1,Day 56,n=19,20	-0.014 (± 0.1783)	0.112 (± 0.2613)		
FEV1,Day 84,n=17,20	-0.029 (± 0.1281)	0.077 (± 0.2747)		
FVC,Day 12,n=20,18	-0.024 (± 0.4723)	0.062 (± 0.3770)		
FVC,Day 28,n=19,20	0.024 (± 0.4159)	0.231 (± 0.4270)		
FVC,Day 56,n=19,20	-0.078 (± 0.4106)	0.212 (± 0.4827)		
FVC,Day 84,n=17,20	-0.104 (± 0.3786)	0.123 (± 0.4579)		

Notes:

[35] - All Subjects Population.

[36] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case Hematology results Post-Baseline relative to Baseline

End point title	Number of participants with worst case Hematology results Post-Baseline relative to Baseline

End point description:

Blood samples were collected to analyze the following s hematology parameters: Hemoglobin, Hematocrit, Mean Corpuscle Hemoglobin (MCH), Mean Corpuscle Volume (MCV), Platelet count, Red Blood Cell (RBC) count, White Blood Cell (WBC) count, Neutrophils, Lymphocytes, Monocytes, Eosinophils and Basophils. Participants were counted in the worst case category that their value changes to (low or high), unless there is no change in their category. Participants whose lab value category was unchanged (example given [e.g.],High to High), or whose value became normal, were not recorded. Participants were counted twice if the participant had values that changed 'To Low' and 'To High', so the percentages may not add to 100%. The value at Screening was considered as Baseline. Data for Worst Case Laboratory Hematology values Post-Baseline Relative to Baseline has been presented.

End point type	Secondary

End point timeframe:

Baseline (Screening) and up to 14 weeks

End point values	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA	NEMI 700 mcg via ELLIPTA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14[37]	14[38]	8[39]	8[40]
Units: Participants				
Basophils,To Low	0	0	0	0
Basophils,To High	0	0	0	0

Eosinophils,To Low	2	4	1	0
Eosinophils,To High	1	1	0	1
Hemoglobin,To Low	0	0	0	0
Hemoglobin,To High	1	0	0	2
Hematocrit,To Low	0	0	0	0
Hematocrit,To High	3	3	0	0
Lymphocytes,To Low	0	1	0	1
Lymphocytes,To High	1	0	0	0
MCH,To Low	0	1	0	0
MCH,To High	1	0	0	1
MCV,To Low	0	0	0	0
MCV,To High	0	0	0	1
Monocytes,To Low	2	3	1	0
Monocytes,To High	0	0	0	1
Total Neutrophils,To Low	0	0	0	0
Total Neutrophils,To High	4	1	2	1
Platelet count,To Low	1	0	1	0
Platelet count,To High	0	1	1	0
RBC,To Low	0	0	0	0
RBC,To High	0	1	0	1
WBC,To Low	1	0	0	0
WBC,To High	4	2	2	1

Notes:

[37] - All Subjects Population.

[38] - All Subjects Population.

[39] - All Subjects Population.

[40] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case Chemistry results Post-Baseline relative to Baseline

End point title	Number of participants with worst case Chemistry results Post-Baseline relative to Baseline

End point description:

Blood samples were collected to analyze the following Chemistry parameters: Albumin, Alkaline Phosphatase (ALP), Alanine Amino Transferase (ALT), Aspartate Amino Transferase (AST), Direct Bilirubin, Total Bilirubin, Calcium, C-Reactive protein, Creatinine, Glucose, Potassium, Sodium, Total Protein and Urea/Blood urea nitrogen. Participants were counted in the worst case category that their value changes to (low, normal or high), unless there is no change in their category. Participants whose lab value category was unchanged e.g. High to High), or whose value became normal, were not recorded. Participants were counted twice if the participant had values that changed 'To Low' and 'To High', so the percentages may not add to 100%. The value at Screening was considered as Baseline. Data for Worst Case Laboratory chemistry values Post-Baseline Relative to Baseline has been presented.

End point type	Secondary

End point timeframe:

Baseline (Screening) and up to 14 weeks

End point values	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA	NEMI 700 mcg via ELLIPTA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14[41]	14[42]	8[43]	8[44]
Units: Participants				
Albumin,To Low	0	0	1	0
Albumin,To High	0	0	0	0
ALP,To Low	0	0	0	0
ALP,To High	0	0	0	1
ALT,To Low	0	0	0	0
ALT,To High	1	0	1	1
AST,To Low	0	0	0	0
AST,To High	0	0	0	0
Direct Bilirubin,To Low	0	0	0	0
Direct Bilirubin,To High	0	0	0	0
Total Bilirubin,To Low	0	0	0	0
Total Bilirubin,To High	1	0	0	0
Calcium,To Low	0	0	0	0
Calcium,To High	0	0	0	0
C-Reactive protein,To Low	0	0	0	0
C-Reactive protein,To High	4	5	3	0
Creatinine,To Low	1	0	1	0
Creatinine,To High	0	1	1	1
Glucose,To Low	1	1	1	0
Glucose,To High	3	2	2	0
Potassium,To Low	0	0	0	0
Potassium,To High	0	0	1	0
Sodium,To Low	0	2	2	0
Sodium,To High	0	0	0	0
Total Protein,To Low	1	1	0	0
Total Protein,To High	0	0	0	0
Urea/BUN,To Low	1	0	0	0
Urea/BUN,To High	0	0	1	1

Notes:

[41] - All Subjects Population.

[42] - All Subjects Population.

[43] - All Subjects Population.

[44] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case Vital Sign results relative to Potential Clinical Importance (PCI) Criteria Post-Baseline relative to Baseline

End point title	Number of participants with worst case Vital Sign results relative to Potential Clinical Importance (PCI) Criteria Post-Baseline relative to Baseline

End point description:

Vital signs were measured in semi-supine position after 5 minutes rest and included Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Heart rate (HR). Data for number of participants with Post-Baseline worst case Vital Sign results relative to PCI Criteria relative to Baseline was presented. PCI ranges were: SBP (lower: <85 and upper: >160 mmHg), DBP (lower: <45 and upper: >100 mmHg),

and HR (lower: <40 and upper: >110 bpm). The value at Screening was considered as Baseline.

End point type	Secondary

End point timeframe:

Baseline (Screening) and up to 14 weeks

End point values	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA	NEMI 700 mcg via ELLIPTA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14[45]	14[46]	8[47]	8[48]
Units: Participants				
SBP, To Low	0	0	0	0
SBP, To High	0	0	0	2
DBP, To Low	0	0	0	0
DBP, To High	0	0	0	0
HR, To Low	0	0	0	0
HR, To High	2	1	0	1

Notes:

[45] - All Subjects Population.

[46] - All Subjects Population.

[47] - All Subjects Population.

[48] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with worst case post-Baseline abnormal Electrocardiogram (ECG) findings

End point title	Number of participants with worst case post-Baseline abnormal Electrocardiogram (ECG) findings

End point description:

A Single 12-lead ECGs was obtained at screening and at each other timepoint during the study using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QT interval corrected using the Fridericia's formula (QTcF) intervals. Data for number of participants with worst case post-Baseline abnormal ECG findings was reported. The value at Screening was considered as Baseline.

End point type	Secondary

End point timeframe:

Up to 14 weeks

End point values	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA	NEMI 700 mcg via ELLIPTA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14[49]	14[50]	8[51]	8[52]
Units: Participants				
Abnormal - not clinically significant	10	7	6	7
Abnormal - clinically significant	0	0	1	0

Notes:

[49] - All Subjects Population.

[50] - All Subjects Population.

[51] - All Subjects Population.

[52] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Adverse Events (AE) and Serious Adverse Events (SAE)

End point title	Number of participants with Adverse Events (AE) and Serious Adverse Events (SAE)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward medical occurrence that at any dose, resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, is associated with liver injury and impaired liver function or any other situation according to medical or scientific judgment was categorized as SAE. Number of participants with AEs and SAEs have been reported.

End point type	Secondary

End point timeframe:

Up to 14 weeks

End point values	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA	NEMI 700 mcg via ELLIPTA
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	14[53]	14[54]	8[55]	8[56]
Units: Participants				
Any AE	11	11	5	5
Any SAE	2	3	4	0

Notes:

[53] - All Subjects Population.

[54] - All Subjects Population.

[55] - All Subjects Population.

[56] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum plasma concentration (Cmax) following administration of NEMI

End point title	Maximum plasma concentration (Cmax) following administration of NEMI

End point description:

Blood samples for pharmacokinetic (PK) analysis was collected at the indicated time points following administration of NEMI via DISKUS and ELLIPTA. Pharmacokinetic Population comprised of participants in all subject population for whom a pharmacokinetic sample was obtained and analyzed. Only those participants with data available at specified time point were analyzed (represented by n=X in category

titles).

End point type	Secondary

End point timeframe:

Day 1: 5 minutes Post-dose on Day 1

End point values	NEMI 1000 mcg via DISKUS	NEMI 700 mcg via ELLIPTA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[57]	7[58]		
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)	508.4 (± 69)	1103.4 (± 34)		

Notes:

[57] - Pharmacokinetic Population.

[58] - Pharmacokinetic Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration following administration of NEMI

End point title	Trough concentration following administration of NEMI

End point description:

Blood samples for pharmacokinetic (PK) analysis was collected at the indicated time points following administration of NEMI via DISKUS and ELLIPTA. 99999 indicates data not available.

End point type	Secondary

End point timeframe:

Day 1: 24 Hours post-dose; Days 12, 28, 56, 84: Pre-dose

End point values	NEMI 1000 mcg via DISKUS	NEMI 700 mcg via ELLIPTA		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	14[59]	8[60]		
Units: Picograms per milliliter				
geometric mean (geometric coefficient of variation)				
Day 1,24 hour, n=8,2	313.9 (± 61)	99999 (± 99999)		
Day 12,pre-dose,n=9,5	1097.1 (± 38)	1077.2 (± 23)		
Day 28,pre-dose, n=9,7	1194.3 (± 76)	1225.8 (± 50)		
Day 56,pre-dose,n=11,7	1155.1 (± 60)	1171.6 (± 49)		
Day 84,pre-dose,n=11,7	1339.6 (± 53)	1058.2 (± 33)		

Notes:

[59] - Pharmacokinetic Population.

[60] - Pharmacokinetic Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in siVaw at FRC and TLC for Individual Regions at Day 28

End point title	Change from Baseline (Day 12) in siVaw at FRC and TLC for Individual Regions at Day 28

End point description:

siVaw is a measure of the volume in an individual's airway corrected for their lobar volume derived from the high resolution computed tomography (HRCT). It was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Baseline (Screening), Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: Milliliters per Liter				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 28,n=16,18	0.996 (0.917 to 1.082)	0.986 (0.907 to 1.072)		
FRC,Scan Trimmed,Lower,Day 28,n=16,18	0.948 (0.862 to 1.042)	1.025 (0.909 to 1.155)		
FRC,Scan Trimmed,Central,Day 28,n=16,18	0.997 (0.955 to 1.042)	1.014 (0.955 to 1.076)		
FRC,Scan Trimmed,Distal,Day 28,n=16,18	0.977 (0.898 to 1.063)	0.996 (0.914 to 1.085)		
FRC,Scan Trimmed,Total,Day 28,n=16,18	0.997 (0.952 to 1.043)	1.012 (0.953 to 1.075)		
TLC,Scan Trimmed,Upper,Day 28,n=17,19	0.973 (0.884 to 1.070)	0.970 (0.930 to 1.012)		
TLC,Scan Trimmed,Lower,Day 28,n=17,19	0.954 (0.865 to 1.051)	0.952 (0.893 to 1.014)		
TLC,Scan Trimmed,Central,Day 28,n=17,19	1.009 (0.979 to 1.040)	0.977 (0.943 to 1.012)		
TLC,Scan Trimmed,Distal,Day 28,n=17,19	0.967 (0.880 to 1.063)	0.960 (0.917 to 1.004)		
TLC,Scan Trimmed,Total,Day 28,n=17,19	1.003 (0.965 to 1.042)	0.972 (0.939 to 1.006)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in iVaw at FRC and TLC for Individual Regions at Day 28

End point title	Change from Baseline (Day 12) in iVaw at FRC and TLC for Individual Regions at Day 28

End point description:

iVaw is a measure of the volume in an individual's airway derived from the HRCT. It was measured at FRC and TLC. Data was collected at longitudinal time points (Untrimmed data): Screening, Day 12 & Day 28 and at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For Untrimmed data and SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[61]	22[62]		
Units: Milliliters				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 28,n=16,18	0.988 (0.912 to 1.070)	0.985 (0.891 to 1.089)		
FRC,Scan Trimmed,Lower,Day 28,n=16,18	0.934 (0.847 to 1.030)	1.010 (0.876 to 1.165)		
FRC,Scan Trimmed,Central,Day 28,n=16,18	0.985 (0.953 to 1.019)	1.008 (0.942 to 1.078)		
FRC,Scan Trimmed,Distal,Day 28,n=16,18	0.966 (0.891 to 1.047)	0.990 (0.890 to 1.102)		
FRC,Scan Trimmed,Total,Day 28,n=16,18	0.985 (0.949 to 1.022)	1.006 (0.938 to 1.080)		
TLC,Scan Trimmed,Upper,Day 28,n=17,19	0.968 (0.877 to 1.067)	0.968 (0.932 to 1.005)		
TLC,Scan Trimmed,Lower,Day 28,n=17,19	0.933 (0.840 to 1.037)	0.942 (0.879 to 1.010)		
TLC,Scan Trimmed,Central,Day 28,n=17,19	0.996 (0.968 to 1.024)	0.972 (0.940 to 1.004)		
TLC,Scan Trimmed,Distal,Day 28,n=17,19	0.954 (0.865 to 1.052)	0.954 (0.912 to 0.998)		
TLC,Scan Trimmed,Total,Day 28,n=17,19	0.989 (0.952 to 1.028)	0.966 (0.936 to 0.998)		

Notes:

[61] - All Subjects Population.

[62] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in iRaw at FRC and TLC for Individual Lobes at Day 28

End point title	Change from Baseline (Day 12) in iRaw at FRC and TLC for Individual Lobes at Day 28

End point description:

iRaw is a measure of the resistance in an individual's airway derived from HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[63]	22[64]		
Units: kPa*s/L				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 28,n=16,18	1.082 (0.714 to 1.641)	1.152 (0.819 to 1.620)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,18	1.266 (0.892 to 1.798)	1.008 (0.641 to 1.587)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,18	1.149 (0.709 to 1.862)	1.477 (0.927 to 2.355)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,18	1.269 (0.840 to 1.916)	1.276 (0.693 to 2.350)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,18	1.768 (0.902 to 3.465)	1.185 (0.759 to 1.850)		
TLC,Scan Trimmed,Right Upper,Day 28,n=17,19	1.133 (0.798 to 1.608)	1.143 (0.995 to 1.314)		
TLC,Scan Trimmed,Left Upper,Day 28,n=17,19	1.000 (0.732 to 1.367)	1.093 (0.927 to 1.288)		
TLC,Scan Trimmed,Right Middle,Day 28,n=17,19	1.971 (0.962 to 4.039)	1.537 (1.055 to 2.238)		
TLC,Scan Trimmed,Right Lower,Day 28,n=17,19	1.408 (0.901 to 2.199)	1.073 (0.779 to 1.478)		
TLC,Scan Trimmed,Left Lower,Day 28,n=17,19	1.486 (0.983 to 2.248)	1.056 (0.691 to 1.615)		

Notes:

[63] - All Subjects Population.

[64] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in iRaw at FRC and TLC for Individual Regions at Day 28

End point title	Change from Baseline (Day 12) in iRaw at FRC and TLC for Individual Regions at Day 28

End point description:

iRaw is a measure of the resistance in an individual's airway derived from HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analyzed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[65]	22[66]		
Units: kPa*s/L				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 28,n=16,18	1.221 (0.870 to 1.715)	1.266 (0.848 to 1.891)		
FRC,Scan Trimmed,Lower,Day 28,n=16,18	1.531 (0.937 to 2.499)	1.278 (0.774 to 2.112)		
FRC,Scan Trimmed,Central,Day 28,n=16,18	0.989 (0.873 to 1.121)	0.926 (0.697 to 1.231)		
FRC,Scan Trimmed,Distal,Day 28,n=16,18	1.373 (0.986 to 1.912)	1.235 (0.856 to 1.781)		
FRC,Scan Trimmed,Total,Day 28,n=16,18	1.157 (0.940 to 1.425)	1.001 (0.714 to 1.402)		
TLC,Scan Trimmed,Upper,Day 28,n=17,19	1.473 (0.938 to 2.313)	1.172 (1.052 to 1.306)		
TLC,Scan Trimmed,Lower,Day 28,n=17,19	1.422 (0.942 to 2.148)	1.089 (0.816 to 1.454)		
TLC,Scan Trimmed,Central,Day 28,n=17,19	0.986 (0.862 to 1.129)	1.044 (0.937 to 1.162)		
TLC,Scan Trimmed,Distal,Day 28,n=17,19	1.712 (1.119 to 2.618)	1.079 (0.883 to 1.319)		
TLC,Scan Trimmed,Total,Day 28,n=17,19	1.321 (0.998 to 1.749)	1.085 (0.933 to 1.263)		

Notes:

[65] - All Subjects Population.

[66] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Lobes at Day 28

End point title	Change from Baseline (Day 12) in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Lobes at Day 28

End point description:

siRaw is a measure of the resistance in an individual's airway corrected for their lobar volume derived from the HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper

lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analysed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[67]	22[68]		
Units: kPa*s				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Right Upper,Day 28,n=16,17	1.079 (0.711 to 1.636)	1.073 (0.794 to 1.451)		
FRC,Scan Trimmed,Left Upper,Day 28,n=16,18	1.249 (0.886 to 1.760)	1.011 (0.653 to 1.566)		
FRC,Scan Trimmed,Right Middle,Day 28,n=16,17	1.097 (0.647 to 1.859)	1.354 (0.885 to 2.070)		
FRC,Scan Trimmed,Right Lower,Day 28,n=16,18	1.241 (0.845 to 1.822)	1.261 (0.706 to 2.252)		
FRC,Scan Trimmed,Left Lower,Day 28,n=16,18	1.760 (0.893 to 3.470)	1.165 (0.755 to 1.798)		
TLC,Scan Trimmed,Right Upper,Day 28,n=17,18	1.132 (0.796 to 1.611)	1.142 (0.977 to 1.336)		
TLC,Scan Trimmed,Left Upper,Day 28,n=17,19	0.992 (0.730 to 1.349)	1.089 (0.921 to 1.288)		
TLC,Scan Trimmed,Right Middle,Day 28,n=17,18	1.915 (0.956 to 3.834)	1.564 (1.042 to 2.347)		
TLC,Scan Trimmed,Right Lower,Day 28,n=17,19	1.380 (0.894 to 2.130)	1.064 (0.783 to 1.447)		
TLC,Scan Trimmed,Left Lower,Day 28,n=17,19	1.453 (0.977 to 2.161)	1.042 (0.683 to 1.590)		

Notes:

[67] - All Subjects Population.

[68] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Regions

End point title	Change from Baseline in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Regions

End point description:

siRaw is a measure of the resistance in an individual’s airway corrected for their lobar volume derived from the HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analysed (represented by n=X1, X2 in the category title). This table presents the SCRD12 scan trim pair data (in rows with

categories containing Scan Trimmed and Day 12) and SCRD28 scan trim pair data (in rows with categories containing Scan Trimmed and Day 28) only.

End point type	Secondary

End point timeframe:

Baseline (Screening) and Days 12 and 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[69]	22[70]		
Units: kPa*s				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 12,n=18,17	0.820 (0.443 to 1.517)	0.828 (0.531 to 1.292)		
FRC,Scan Trimmed,Upper,Day 28,n=16,19	1.377 (0.679 to 2.793)	0.784 (0.546 to 1.124)		
FRC,Scan Trimmed,Lower,Day 12,n=17,17	1.118 (0.559 to 2.239)	1.043 (0.516 to 2.109)		
FRC,Scan Trimmed,Lower,Day 28,n=16,19	1.073 (0.529 to 2.177)	0.891 (0.601 to 1.321)		
FRC,Scan Trimmed,Central,Day 12,n=18,17	0.931 (0.634 to 1.367)	0.878 (0.734 to 1.050)		
FRC,Scan Trimmed,Central,Day 28,n=16,19	0.870 (0.598 to 1.265)	0.867 (0.709 to 1.060)		
FRC,Scan Trimmed,Distal,Day 12,n=18,17	0.999 (0.617 to 1.617)	1.085 (0.567 to 2.077)		
FRC,Scan Trimmed,Distal,Day 28,n=16,19	1.161 (0.566 to 2.380)	0.853 (0.604 to 1.204)		
FRC,Scan Trimmed,Total,Day 12,n=18,17	0.983 (0.674 to 1.435)	0.961 (0.717 to 1.287)		
FRC,Scan Trimmed,Total,Day 28,n=16,19	1.038 (0.656 to 1.641)	0.909 (0.719 to 1.150)		
TLC,Scan Trimmed,Upper,Day 12,n=20,18	1.139 (0.886 to 1.464)	1.156 (0.723 to 1.849)		
TLC,Scan Trimmed,Upper,Day 28,n=18,20	1.524 (1.101 to 2.111)	1.257 (0.950 to 1.664)		
TLC,Scan Trimmed,Lower,Day 12,n=20,18	0.878 (0.665 to 1.161)	1.179 (0.822 to 1.690)		
TLC,Scan Trimmed,Lower,Day 28,n=18,20	1.142 (0.740 to 1.760)	1.282 (0.982 to 1.673)		
TLC,Scan Trimmed,Central,Day 12,n=20,18	0.994 (0.883 to 1.120)	0.990 (0.870 to 1.127)		
TLC,Scan Trimmed,Central,Day 28,n=18,20	0.978 (0.904 to 1.059)	1.039 (0.931 to 1.160)		
TLC,Scan Trimmed,Distal,Day 12,n=20,18	0.966 (0.735 to 1.271)	1.259 (0.815 to 1.946)		
TLC,Scan Trimmed,Distal,Day 28,n=18,20	1.323 (0.869 to 2.014)	1.266 (0.981 to 1.633)		
TLC,Scan Trimmed,Total,Day 12,n=20,18	1.000 (0.840 to 1.191)	1.093 (0.844 to 1.416)		
TLC,Scan Trimmed,Total,Day 28,n=18,20	1.188 (0.958 to 1.473)	1.181 (0.978 to 1.427)		

Notes:

[69] - All Subjects Population.

[70] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline (Day 12) in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Regions at Day 28

End point title	Change from Baseline (Day 12) in Specific Imaging Airway Resistance (siRaw) at FRC and TLC for Individual Regions at Day 28

End point description:

siRaw is a measure of the resistance in an individual's airway corrected for their lobar volume derived from the HRCT. It was measured at FRC and TLC. Data was collected at each time point for scan trimmed pairs: SCRD12, SCRD28 & D12D28. At each time point it was measure at 5 lobes (right upper lobe, left upper lobe, right middle lobe, right lower lobe & left lower lobe) and 5 Regions (Upper, Lower, Central, Distal & Total). For SCRD12 & SCRD28 scan trimmed pairs the baseline is screening, for D12D28 scan trimmed pair the baseline is D12. Change from baseline is the post-Baseline value minus the Baseline value. Only participants available at the specified time point were analysed (represented by n=X1, X2 in the category title). This table presents the D12D28 scan trim pair data only.

End point type	Secondary

End point timeframe:

Baseline (Day 12) and Day 28

End point values	All Placebo	All NEMI		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[71]	22[72]		
Units: kPa*s				
geometric mean (confidence interval 95%)				
FRC,Scan Trimmed,Upper,Day 28,n=16,18	1.211 (0.852 to 1.722)	1.265 (0.872 to 1.836)		
FRC,Scan Trimmed,Lower,Day 28,n=16,18	1.508 (0.929 to 2.448)	1.260 (0.778 to 2.041)		
FRC,Scan Trimmed,Central,Day 28,n=16,18	0.977 (0.861 to 1.110)	0.921 (0.703 to 1.206)		
FRC,Scan Trimmed,Distal,Day 28,n=16,18	1.356 (0.980 to 1.877)	1.227 (0.876 to 1.720)		
FRC,Scan Trimmed,Total,Day 28,n=16,18	1.144 (0.922 to 1.418)	0.995 (0.723 to 1.368)		
TLC,Scan Trimmed,Upper,Day 28,n=17,19	1.465 (0.934 to 2.300)	1.169 (1.050 to 1.302)		
TLC,Scan Trimmed,Lower,Day 28,n=17,19	1.392 (0.936 to 2.072)	1.079 (0.813 to 1.430)		
TLC,Scan Trimmed,Central,Day 28,n=17,19	0.973 (0.853 to 1.111)	1.038 (0.935 to 1.153)		
TLC,Scan Trimmed,Distal,Day 28,n=17,19	1.689 (1.111 to 2.567)	1.073 (0.882 to 1.305)		
TLC,Scan Trimmed,Total,Day 28,n=17,19	1.303 (0.990 to 1.717)	1.079 (0.932 to 1.250)		

Notes:

[71] - All Subjects Population.

[72] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from the start of study treatment until the follow up (Up to 14 weeks)

Adverse event reporting additional description:

All Subjects Population was used to collect Adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Placebo via DISKUS

Reporting group description:

Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI

Reporting group title	NEMI 1000 mcg via DISKUS

Reporting group description:

Participants were administered with NEMI 1000 mcg once daily in the morning before breakfast for 84 consecutive days using DISKUS DPI.

Reporting group title	Placebo via ELLIPTA

Reporting group description:

Participants were administered with placebo matching NEMI once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI

Reporting group title	NEMI 700 mcg via ELLIPTA

Reporting group description:

Participants were administered with NEMI 700 mcg once daily in the morning before breakfast for 84 consecutive days using ELLIPTA DPI.

Serious adverse events	Placebo via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	3 / 14 (21.43%)	4 / 8 (50.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (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
Cardiac disorders			
Coronary artery disease			

subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
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			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (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
Laryngospasm			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (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
Pulmonary oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	2 / 8 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	NEMI 700 mcg via ELLIPTA		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Oxygen saturation decreased			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery disease			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Laryngospasm			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 8 (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 via DISKUS	NEMI 1000 mcg via DISKUS	Placebo via ELLIPTA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 14 (71.43%)	10 / 14 (71.43%)	5 / 8 (62.50%)
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Chills			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Drug intolerance			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 14 (21.43%)	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	3	2	1
Cough			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Bronchospasm			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pneumonia aspiration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Sinus congestion			

subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Depressive symptom			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood magnesium decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 14 (7.14%)	4 / 14 (28.57%)	1 / 8 (12.50%)
occurrences (all)	1	10	1
Aphonia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	2 / 8 (25.00%)
occurrences (all)	0	1	2
Toothache			
subjects affected / exposed	0 / 14 (0.00%)	2 / 14 (14.29%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 14 (21.43%)	2 / 14 (14.29%)	0 / 8 (0.00%)
occurrences (all)	3	2	0
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Rash erythematous			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal pain			
subjects affected / exposed	2 / 14 (14.29%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Pain in extremity			
subjects affected / exposed	2 / 14 (14.29%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	4	0	0
Joint swelling			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Oral herpes			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Oral candidiasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Periorbital cellulitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 14 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	0 / 8 (0.00%)
occurrences (all)	0	1	0

Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 14 (7.14%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Hypokalaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	2 / 8 (25.00%)
occurrences (all)	0	0	2
Hypoglycaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Hypophosphataemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 14 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1

Non-serious adverse events	NEMI 700 mcg via ELLIPTA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 8 (62.50%)		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Chills			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Drug intolerance			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Cough			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	2		
Oropharyngeal pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Bronchospasm			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pneumonia aspiration			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Depressive symptom			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

Panic attack subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Investigations Blood magnesium decreased subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Aphonia subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 8 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper	0 / 8 (0.00%) 0 0 / 8 (0.00%) 0 0 / 8 (0.00%) 0		

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Drug eruption			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Rash erythematous			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Neck pain			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)		
occurrences (all)	2		
Oral herpes			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Periorbital cellulitis			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Pneumonia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			

subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 8 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 November 2015	Amendment No. 1: Remove the specific equations for the prediction of percent predicted from spirometry from the inclusion criteria and in Section 7.7.2. At screening it may not be possible to identify which correction method was used, at the time. It therefore is not valid to stipulate that lung function values be corrected using any particular method. Both Forced expiratory Volume (FEV1) and Forced vital Capacity (FVC) measurements (which are not entry criteria for the study) collected during the study will be collected as absolute values (uncorrected), so that consistency will be obtained across all sites in the study, and percent predicted will be calculated using a standard approach in house at the end of the study.
26 January 2016	Amendment No. 2: Increase the Body Mass Index (BMI) range in the inclusion criteria from 18-32 kg/m^2 (inclusive) t The original BMI range from 16 – 35 kg/m^2 is a typical range used in both healthy volunteer studies and general participant populations. The revised range is more appropriate for a COPD participant population.
16 November 2016	Amendment No. 3: To remove the photo-toxicity from the protocol and to include minor administrative and clarification changes.
22 March 2017	Amendment No. 4: Replace the administration of GSK2269557 via the DISKUS device [1000 micrograms (mcg)] by a comparable dose administered via the ELLIPTA device (700 mcg). GSK2269557 is no longer manufactured for use with the DISKUS device which will be replaced with ELLIPTA Device. To increase the number of participants to be recruited to obtain sufficient completers. Minor updates and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported