EU Clinical Trials Register

Clinical trial results:
An open label, randomised, parallel group clinical study to evaluate the effect of the Connected Inhaler System (CIS) on adherence to Relvar/Breo ELLIPTA therapy, in asthmatic subjects with poor control

Summary

EudraCT number	2017-002266-45
Trial protocol	GB DE NL ES FR IT
Global end of trial date	24 January 2019

Results information

Result version number	v1 (current)
This version publication date	08 February 2020
First version publication date	08 February 2020

Trial information

Trial identification

Sponsor protocol code	207040

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	08 May 2019

Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 January 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the effect of 6 months use of the CIS on adherence to ELLIPTA maintenance therapy when both the subject and the HCP are supplied with data from the maintenance sensor versus no data supplied to the subject and HCP (Arm 1 vs Arm 5)

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2018
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: 127
Country: Number of subjects enrolled	Germany: 63
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Netherlands: 34
Country: Number of subjects enrolled	Spain: 45
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	United States: 112
Worldwide total number of subjects	437
EEA total number of subjects	198

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)	380
From 65 to 84 years	56
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This was an open-label, randomized, multi-center, parallel group study to evaluate the effect of the connected inhaler system (CIS) on adherence to Relvar/Breo ELLIPTA therapy, in asthmatic participants (Par) with poor control.

Pre-assignment

Screening details:

A total of 528 participants were screened and 437 participants were enrolled and randomized in this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1: Data on maintenance use supplied to Par and HCP

Arm description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 microgram (mcg) or 200/25 mcg per actuation administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via metered dose inhaler (MDI), as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant via an application on smart phone and to the participant's healthcare professional (HCP) via an online dashboard.

Arm type	Experimental
Investigational medicinal product name	Relvar/Breo ELLIPTA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Relvar/Breo maintenance therapy was available at doses of 100/25 microgram (mcg) and 200/25 mcg administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily

Investigational medicinal product name	Salbutamol MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol rescue medication was available at dose of 100 mcg administered via metered dose inhaler (MDI), as and when required

Arm title	Cohort 2: Data on maintenance use supplied to Par

Arm description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant only via an application on smart phone.

Arm type	Experimental

Investigational medicinal product name	Relvar/Breo ELLIPTA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Relvar/Breo maintenance therapy was available at doses of 100/25 microgram (mcg) and 200/25 mcg administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily

Investigational medicinal product name	Salbutamol MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol rescue medication was available at dose of 100 mcg administered via metered dose inhaler (MDI), as and when required

Arm title	Cohort 3: Data on maintenance and rescue use to Par and HCP

Arm description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone and to HCP via an online dashboard.

Arm type	Experimental
Investigational medicinal product name	Relvar/Breo ELLIPTA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Relvar/Breo maintenance therapy was available at doses of 100/25 microgram (mcg) and 200/25 mcg administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily

Investigational medicinal product name	Salbutamol MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol rescue medication was available at dose of 100 mcg administered via metered dose inhaler (MDI), as and when required

Arm title	Cohort 4: Data on maintenance and rescue use supplied to Par

Arm description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone.

Arm type	Experimental
Investigational medicinal product name	Relvar/Breo ELLIPTA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Relvar/Breo maintenance therapy was available at doses of 100/25 microgram (mcg) and 200/25 mcg administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily

Investigational medicinal product name	Salbutamol MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol rescue medication was available at dose of 100 mcg administered via metered dose inhaler (MDI), as and when required

Arm title	Cohort 5: No data supplied to Par or HCP

Arm description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Participants were provided with a home hub through which their data was uploaded during the study but the participants and their HCP were not able to view the data.

Arm type	Experimental
Investigational medicinal product name	Relvar/Breo ELLIPTA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Relvar/Breo maintenance therapy was available at doses of 100/25 microgram (mcg) and 200/25 mcg administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily

Investigational medicinal product name	Salbutamol MDI
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Salbutamol rescue medication was available at dose of 100 mcg administered via metered dose inhaler (MDI), as and when required

Number of subjects in period 1	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP
Started	87	88	88
Completed	82	81	77
Not completed	5	7	11
Protocol deviation	1	-	1
Physician decision	-	1	-
Lack of efficacy	-	-	-
Adverse event, non-fatal	1	1	1
Consent withdrawn by subject	3	3	5
Lost to follow-up	-	2	4

Number of subjects in period 1	Cohort 4: Data on maintenance and rescue use supplied to Par	Cohort 5: No data supplied to Par or HCP
Started	88	86
Completed	78	81
Not completed	10	5
Protocol deviation	-	1
Physician decision	1	1
Lack of efficacy	2	1
Adverse event, non-fatal	2	-
Consent withdrawn by subject	2	1
Lost to follow-up	3	1

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Data on maintenance use supplied to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 microgram (mcg) or 200/25 mcg per actuation administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via metered dose inhaler (MDI), as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant via an application on smart phone and to the participant's healthcare professional (HCP) via an online dashboard.

Reporting group title	Cohort 2: Data on maintenance use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant only via an application on smart phone.

Reporting group title	Cohort 3: Data on maintenance and rescue use to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone and to HCP via an online dashboard.

Reporting group title	Cohort 4: Data on maintenance and rescue use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone.

Reporting group title	Cohort 5: No data supplied to Par or HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Participants were provided with a home hub through which their data was uploaded during the study but the participants and their HCP were not able to view the data.

Reporting group values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP
Number of subjects	87	88	88
Age categorical			
Units: Subjects			
Total Participants	87	88	88
Age Continuous			
Units: Years			
arithmetic mean	46.7	47.0	47.8
standard deviation	± 15.79	± 14.70	± 15.28

Sex: Female, Male			
Units: Participants			
Female	64	54	59
Male	23	34	29
Race/Ethnicity, Customized			
Units: Subjects			
American Indian (AI) or Alaska native (AN)	1	0	0
Asian-Central/South Asian Heritage	1	3	1
Asian-East Asian Heritage	1	0	0
Asian-South East (SE) Asian Heritage (AH)	2	2	3
Black or African American	10	3	8
Native Hawaiian or other Pacific Islander	0	1	0
White-Arabic/North African heritage	0	0	0
White-White/Caucasian/European Heritage (EH)	72	76	76
AI or AN and Black or African American	0	2	0
AI or AN and White-White/Caucasian/EH	0	1	0
Asian-SE AH and White-White/Caucasian/EH	0	0	0

Reporting group values	Cohort 4: Data on maintenance and rescue use supplied to Par	Cohort 5: No data supplied to Par or HCP	Total
Number of subjects	88	86	437
Age categorical			
Units: Subjects			
Total Participants	88	86	437
Age Continuous			
Units: Years			
arithmetic mean	47.8	47.2	
standard deviation	± 13.23	± 15.91	-
Sex: Female, Male			
Units: Participants			
Female	60	47	284
Male	28	39	153
Race/Ethnicity, Customized			
Units: Subjects			
American Indian (AI) or Alaska native (AN)	0	2	3
Asian-Central/South Asian Heritage	2	1	8
Asian-East Asian Heritage	0	1	2
Asian-South East (SE) Asian Heritage (AH)	2	3	12
Black or African American	9	4	34
Native Hawaiian or other Pacific Islander	0	0	1
White-Arabic/North African heritage	1	1	2
White-White/Caucasian/European Heritage (EH)	74	73	371

AI or AN and Black or African American	0	0	2
AI or AN and White-White/Caucasian/EH	0	0	1
Asian-SE AH and White-White/Caucasian/EH	0	1	1

End points

End points reporting groups

Reporting group title	Cohort 1: Data on maintenance use supplied to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 microgram (mcg) or 200/25 mcg per actuation administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via metered dose inhaler (MDI), as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant via an application on smart phone and to the participant's healthcare professional (HCP) via an online dashboard.

Reporting group title	Cohort 2: Data on maintenance use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant only via an application on smart phone.

Reporting group title	Cohort 3: Data on maintenance and rescue use to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone and to HCP via an online dashboard.

Reporting group title	Cohort 4: Data on maintenance and rescue use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone.

Reporting group title	Cohort 5: No data supplied to Par or HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Participants were provided with a home hub through which their data was uploaded during the study but the participants and their HCP were not able to view the data.

Primary: Percentage of ELLIPTA doses taken (daily adherence) between Month 4 and Month 6 as determined by the maintenance sensor for arms; ("cohort 1: data on maintenance use supplied to participant and HCP" and "Cohort 5: no data supplied to participant or HCP")

End point title	Percentage of ELLIPTA doses taken (daily adherence) between Month 4 and Month 6 as determined by the maintenance sensor for arms; ("cohort 1: data on maintenance use supplied to participant and HCP" and "Cohort 5: no data supplied to participant or HCP")[1]

End point description:

Daily adherence is defined as the participant taking one dose of Relvar/Breo ELLIPTA, within a 24-hour period, starting at 12.00 anti-meridiem (a.m.) each day of the treatment period. The percentage of ELLIPTA doses taken were determined by the clip-on sensor attached to ELLIPTA, which records the time

and date when the ELLIPTA cover was opened and closed. Least Square mean percentage of ELLIPTA doses taken was determined by the maintenance sensor daily adherence over the last three months of the study period (between months 4 to 6). The daily adherence to ELLIPTA maintenance therapy when both the participant and the HCP were supplied with data from the maintenance sensor (Cohort 1) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Intent-to-Treat (ITT) Population comprised of all randomized participants, excluding those who were randomized in error. Only those participants with adherence data observed/imputed at the specified time points were analyzed.

End point type	Primary

End point timeframe:	
Month 4 to Month 6	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 5: No data supplied to Par or HCP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	83[2]	85[3]		
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	80.9 (± 3.19)	69.0 (± 3.19)		

Notes:

[2] - ITT Population

[3] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	168
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	12
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.2
upper limit	18.8

Notes:

[4] - p-value was calculated using ANCOVA.

Secondary: Percentage of ELLIPTA doses taken (daily adherence) between Month 4 and Month 6 as determined by the maintenance sensor

End point title	Percentage of ELLIPTA doses taken (daily adherence) between

	Month 4 and Month 6 as determined by the maintenance sensor[5]

End point description:

Daily adherence is defined as the participant taking one dose of Relvar/Breo ELLIPTA, within a 24-hour period, starting at 12.00 a.m. each day of the treatment period. The percentage of ELLIPTA doses taken were determined by the clip-on sensor attached to ELLIPTA, which records the time and date when the ELLIPTA cover was opened and closed. Least Square mean percentage of ELLIPTA doses taken (daily adherence) was determined by the maintenance sensor daily adherence over the last three months of the study period (between months 4 to 6). The effect on daily adherence to maintenance therapy when maintenance data was only supplied to participants (Cohort 2), rescue and maintenance data were supplied to participant and HCP (Cohort 3), and rescue and maintenance data only supplied to participant (Cohort 4) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Only those participants with adherence data observed/imputed at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Month 4 to Month 6

Notes:

[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: This endpoint is only reporting on a subset of the arms that are contained in the Baseline period.

End point values	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par	Cohort 5: No data supplied to Par or HCP
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	84[6]	84[7]	82[8]	85[9]
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	77.2 (± 3.04)	78.3 (± 3.11)	77.1 (± 3.25)	69.0 (± 3.19)

Notes:

[6] - ITT Population

[7] - ITT Population

[8] - ITT Population

[9] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	other[10]
P-value	= 0.016
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	14.9

Notes:

[10] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.	
Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	169
Analysis specification	Pre-specified
Analysis type	other[11]
P-value	= 0.006
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.7
upper limit	16

Notes:

[11] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.	
Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	other[12]
P-value	= 0.018
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	14.8

Notes:

[12] - p-value was calculated using ANCOVA.

Secondary: Percentage of ELLIPTA doses taken (daily adherence) between Month 1 and Month 3 as determined by the maintenance sensor

End point title	Percentage of ELLIPTA doses taken (daily adherence) between Month 1 and Month 3 as determined by the maintenance sensor
End point description:	
Daily adherence is defined as the participant taking one dose of Relvar/Breo ELLIPTA, within a 24-hour	

period, starting at 12.00 a.m. each day of the treatment period. The percentageof ELLIPTA doses taken were determined by the clip-on sensor attached to ELLIPTA, which records the time and date when the ELLIPTA cover was opened and closed. Least Square mean percentage of ELLIPTA doses taken (daily adherence) was determined by the maintenance sensor daily adherence. The effect on daily adherence to maintenance therapy when maintenance data was supplied to both the participant and the HCP (Cohort 1), maintenance data was only supplied to participants (Cohort 2), rescue and maintenance data were supplied to participant and HCP (Cohort 3), and rescue and maintenance data only supplied to participant (Cohort 4) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Only those participants with adherence data observed/imputed at the specified time points were analyzed.

End point type	Secondary

End point timeframe:
Month 1 to Month 3

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[13]	87[14]	88[15]	88[16]
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	85.7 (± 2.82)	84.2 (± 2.66)	82.0 (± 2.74)	79.2 (± 2.78)

Notes:

[13] - ITT Population

[14] - ITT Population

[15] - ITT Population

[16] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	86[17]			
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	76.4 (± 2.82)			

Notes:

[17] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:
Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other[18]
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	3.2
upper limit	15.3

Notes:

[18] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[19]
P-value	= 0.011
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	13.7

Notes:

[19] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[20]
P-value	= 0.066
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.4
upper limit	11.4

Notes:

[20] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[21]
P-value	= 0.359
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	8.7

Notes:

[21] - p-value was calculated using ANCOVA.

Secondary: Percentage of ELLIPTA doses taken (daily adherence) between Month 1 and Month 6 as determined by the maintenance sensor

End point title	Percentage of ELLIPTA doses taken (daily adherence) between Month 1 and Month 6 as determined by the maintenance sensor

End point description:

Daily adherence is defined as the participant taking one dose of Relvar/Breo ELLIPTA, within a 24-hour period, starting at 12.00 a.m. each day of the treatment period. Least Square mean percentage of ELLIPTA doses taken (daily adherence) between Months 1 and 6 was determined by the maintenance sensor daily adherence. The effect on daily adherence to maintenance therapy when maintenance data was supplied to both the participant and the HCP (Cohort 1), maintenance data was only supplied to participants (Cohort 2), rescue and maintenance data were supplied to participant and HCP (Cohort 3), and rescue and maintenance data only supplied to participant (Cohort 4) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Only those participants with adherence data observed/imputed at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Month 1 to Month 6

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	86[22]	87[23]	88[24]	88[25]
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	81.5 (± 3.07)	78.8 (± 2.90)	77.7 (± 2.99)	75.2 (± 3.03)

Notes:

[22] - ITT Population

[23] - ITT Population

[24] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	86[26]			
Units: Percentage of ELLIPTA doses				
least squares mean (standard error)	71.8 (± 3.07)			

Notes:

[26] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.	
Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other[27]
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.1
upper limit	16.3

Notes:

[27] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.	
Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[28]
P-value	= 0.032
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided

lower limit	0.6
upper limit	13.5

Notes:

[28] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[29]
P-value	= 0.07
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	12.4

Notes:

[29] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline adherence, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.294
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3
upper limit	9.9

Notes:

[30] - p-value was calculated using ANCOVA.

Secondary: Percentage of rescue free days between Month 4 and Month 6 as determined by the rescue medication sensor

End point title	Percentage of rescue free days between Month 4 and Month 6 as determined by the rescue medication sensor
End point description:	

Data for rescue medication use was collected by the clip-on sensor for salbutamol MDI which records time and date when the MDI was actuated. Percentage of rescue free days were determined by the rescue sensor records of date, time and number of inhaler actuations. Least Square mean percentage of rescue free days between Months 4 and 6 when maintenance data was supplied to both the participant and the HCP (Cohort 1); maintenance data was only supplied to participants (Cohort 2); rescue and maintenance data were supplied to participant and HCP (Cohort 3) and rescue and maintenance data only supplied to participant (Cohort 4) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Only those participants with rescue data observed/imputed at the specified time points were analyzed.

End point type	Secondary

End point timeframe:	
Month 4 to Month 6	

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87[31]	88[32]	88[33]	88[34]
Units: Percentage of rescue free days				
least squares mean (standard error)	81.1 (± 2.82)	81.2 (± 2.66)	85.6 (± 2.76)	83.7 (± 2.80)

Notes:

[31] - ITT Population

[32] - ITT Population

[33] - ITT Population

[34] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	85[35]			
Units: Percentage of rescue free days				
least squares mean (standard error)	76.4 (± 2.82)			

Notes:

[35] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline rescue use, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	172
Analysis specification	Pre-specified
Analysis type	other[36]
P-value	= 0.118
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	10.8

Notes:

[36] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline rescue use, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[37]
P-value	= 0.105
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	10.7

Notes:

[37] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline rescue use, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[38]
P-value	= 0.002
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	15.1

Notes:

[38] - p-value was calculated using ANCOVA.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:	

Analysis was performed by ANCOVA adjusted for randomized treatment arm, Baseline rescue use, duration of run-in (visits), country, gender and age.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.015
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	13.2

Notes:

[39] - p-value was calculated using ANCOVA.

Secondary: Number of doses of rescue medication use between Month 4 and Month 6 as determined by the rescue medication sensor

End point title	Number of doses of rescue medication use between Month 4 and Month 6 as determined by the rescue medication sensor

End point description:

Data for rescue medication use was collected by the clip-on sensor for salbutamol MDI which records time and date when the MDI was actuated. Total rescue use was determined by the rescue sensor records of date, time and number of inhaler actuations. The mean number of doses of rescue medicines between Months 4 and 6 when maintenance data was supplied to both the participant and the HCP (Cohort 1); maintenance data was only supplied to participants (Cohort 2); rescue and maintenance data were supplied to participant and HCP (Cohort 3) and rescue and maintenance data only supplied to participant (Cohort 4) versus no data supplied to the participant or HCP (Cohort 5) is summarized. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Month 4 to Month 6

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	83[40]	84[41]	85[42]	82[43]
Units: Doses of rescue medication				
arithmetic mean (standard deviation)	55.3 (± 107.73)	40.6 (± 91.53)	29.5 (± 54.41)	27.0 (± 45.27)

Notes:

[40] - ITT Population

[41] - ITT Population

[42] - ITT Population

[43] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	85[44]			
Units: Doses of rescue medication				
arithmetic mean (standard deviation)	55.8 (± 158.49)			

Notes:

[44] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in asthma control test (ACT) total score

End point title	Change from Baseline in asthma control test (ACT) total score

End point description:

The ACT is a validated self-completed questionnaire utilizing 5 questions to assess asthma control on a 5-point categorical scale ranging from 1 (not controlled at all) to 5 (completely controlled). Total score is calculated as the sum of the scores from the 5 questions and can range from 5 to 25, with higher scores indicating better control. An ACT total score of 5 to 19 suggests that the participant's asthma is unlikely to be well controlled, whilst a score of 20 to 25 suggests that the participant's asthma is likely to be well controlled. Baseline value was the latest assessment prior to randomization (Day 1, pre-dose). Change from Baseline was calculated as post-dose visit value minus the Baseline value. Only those participants with data available at the specified data points were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Month 6

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	82[45]	82[46]	78[47]	78[48]
Units: Scores on a Scale				
least squares mean (standard error)	3.4 (± 0.40)	4.3 (± 0.40)	4.7 (± 0.41)	4.2 (± 0.41)

Notes:

[45] - ITT Population

[46] - ITT Population

[47] - ITT Population

[48] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	82[49]			
Units: Scores on a Scale				
least squares mean (standard error)	3.9 (± 0.40)			

Notes:

[49] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by MMRM adjusted for randomized treatment arm,Baseline ACT total score,randomized treatment arm-by-visit interaction,Baseline ACT total score-by-visit interaction,gender,age,country and participant fitted as a random factor.

Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	other[50]
P-value	= 0.4
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	0.6

Notes:

[50] - p-value was calculated using Mixed Model Repeated Measures (MMRM).

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by MMRM adjusted for randomized treatment arm,Baseline ACT total score,randomized treatment arm-by-visit interaction,Baseline ACT total score-by-visit interaction,gender,age,country and participant fitted as a random factor.

Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	164
Analysis specification	Pre-specified
Analysis type	other[51]
P-value	= 0.441
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	1.5

Notes:

[51] - p-value was calculated using MMRM.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by MMRM adjusted for randomized treatment arm,Baseline ACT total score,randomized treatment arm-by-visit interaction,Baseline ACT total score-by-visit interaction,gender,age,country and participant fitted as a random factor.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	= 0.164
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	1.9

Notes:

[52] - p-value was calculated using MMRM.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by MMRM adjusted for randomized treatment arm,Baseline ACT total score,randomized treatment arm-by-visit interaction,Baseline ACT total score-by-visit interaction,gender,age,country and participant fitted as a random factor.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	160
Analysis specification	Pre-specified
Analysis type	other[53]
P-value	= 0.661
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.4

Notes:

[53] - p-value was calculated using MMRM.

Secondary: Percentage of participants attaining asthma control (percentage of participants with an ACT total score >=20) at Month 6

End point title	Percentage of participants attaining asthma control (percentage of participants with an ACT total score >=20) at Month 6

End point description:

Percentage of participants attaining asthma control was defined as participants with an ACT total score >=20 at Month 6. The ACT is a validated self-completed questionnaire utilizing 5 questions to assess asthma control on a 5-point categorical scale ranging from 1 (not controlled at all) to 5 (completely controlled). Total score is calculated as the sum of the scores from the 5 questions and can range from 5

to 25, with higher scores indicating better control. An ACT total score of 5 to 19 suggests that the participant's asthma is unlikely to be well controlled, whilst a score of 20 to 25 suggests that the participant's asthma is likely to be well controlled. Percentage of participants who attained asthma control at Month 6 is presented.

End point type	Secondary
End point timeframe:	
Month 6	

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87[54]	88[55]	88[56]	88[57]
Units: Percentage of participants	52	66	55	53

Notes:

[54] - ITT Population

[55] - ITT Population

[56] - ITT Population

[57] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	86[58]			
Units: Percentage of participants	62			

Notes:

[58] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[59]
P-value	= 0.385
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.44

Notes:

[59] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[60]
P-value	= 0.517
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	2.42

Notes:

[60] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[61]
P-value	= 0.921
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.51
upper limit	1.85

Notes:

[61] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174

Analysis specification	Pre-specified
Analysis type	other[62]
P-value	= 0.321
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	1.38

Notes:

[62] - p-value was calculated using logistic regression

Secondary: Percentage of participants with an increase from Baseline >=3 in ACT total score at Month 6

End point title	Percentage of participants with an increase from Baseline >=3 in ACT total score at Month 6

End point description:

The ACT is a validated self-completed questionnaire utilizing 5 questions to assess asthma control on a 5-point categorical scale ranging from 1 (not controlled at all) to 5 (completely controlled). Total score is calculated as the sum of the scores from the 5 questions and can range from 5 to 25, with higher scores indicating better control. An ACT total score of 5 to 19 suggests that the participant's asthma is unlikely to be well controlled, whilst a score of 20 to 25 suggests that the participant's asthma is likely to be well controlled. Baseline value was the latest assessment prior to randomization (Day 1, pre-dose). Percentage of participants with an increase from Baseline >=3 in ACT total score at Month 6 is presented.

End point type	Secondary

End point timeframe:

Baseline and Month 6

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87[63]	88[64]	88[65]	88[66]
Units: Percentage of participants	61	69	65	63

Notes:

[63] - ITT Population

[64] - ITT Population

[65] - ITT Population

[66] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	86[67]			
Units: Percentage of participants	64			

Notes:

[67] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[68]
P-value	= 0.911
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.98

Notes:

[68] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.	
Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[69]
P-value	= 0.383
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	2.54

Notes:

[69] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[70]
P-value	= 0.814
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.04

Notes:

[70] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[71]
P-value	= 0.986
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	1.89

Notes:

[71] - p-value was calculated using logistic regression

Secondary: Percentage of participants who have either an ACT total score of >=20 and/or an increase from Baseline >=3 in ACT total score at Month 6

End point title	Percentage of participants who have either an ACT total score of >=20 and/or an increase from Baseline >=3 in ACT total score at Month 6

End point description:

The ACT is a validated self-completed questionnaire utilizing 5 questions to assess asthma control on a 5-point categorical scale ranging from 1 (not controlled at all) to 5 (completely controlled). Total score is calculated as the sum of the scores from the 5 questions and can range from 5 to 25, with higher scores indicating better control. Baseline value was the latest assessment prior to randomization (Day 1, pre-dose). Percentage of participants who had either an ACT total score of >=20 and/or an increase from Baseline >=3 in ACT total score at Month 6 is presented.

End point type	Secondary

End point timeframe:

Baseline and Month 6

End point values	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP	Cohort 4: Data on maintenance and rescue use supplied to Par
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87[72]	88[73]	88[74]	88[75]
Units: Percentage of participants	66	75	65	67

Notes:

[72] - ITT Population

[73] - ITT Population

[74] - ITT Population

[75] - ITT Population

End point values	Cohort 5: No data supplied to Par or HCP			
Subject group type	Reporting group			
Number of subjects analysed	86[76]			
Units: Percentage of participants	70			

Notes:

[76] - ITT Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 1: Data on maintenance use supplied to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	173
Analysis specification	Pre-specified
Analysis type	other[77]
P-value	= 0.833
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.81

Notes:

[77] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 2: Data on maintenance use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[78]
P-value	= 0.383
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	2.67

Notes:

[78] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 3: Data on maintenance and rescue use to Par and HCP v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[79]
P-value	= 0.628
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	1.63

Notes:

[79] - p-value was calculated using logistic regression

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Analysis was performed by logistic regression adjusted for randomized treatment arm, Baseline ACT total score, country, gender and age.

Comparison groups	Cohort 4: Data on maintenance and rescue use supplied to Par v Cohort 5: No data supplied to Par or HCP
Number of subjects included in analysis	174
Analysis specification	Pre-specified
Analysis type	other[80]
P-value	= 0.844
Method	Regression, Logistic

Parameter estimate	Odds ratio (OR)
Point estimate	0.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.8

Notes:

[80] - p-value was calculated using logistic regression

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study treatment up to 6 months

Adverse event reporting additional description:

SAEs and non-serious AEs were reported for the ITT Population which comprised of all randomized participants, excluding those who were randomized in error.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Cohort 1: Data on maintenance use supplied to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 microgram (mcg) or 200/25 mcg per actuation administered via ELLIPTA dry powder inhaler (DPI), one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via metered dose inhaler (MDI), as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant via an application on smart phone and to the participant's healthcare professional (HCP) via an online dashboard.

Reporting group title	Cohort 2: Data on maintenance use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensor attached to Relvar/Breo ELLIPTA was fed back to the participant only via an application on smart phone.

Reporting group title	Cohort 3: Data on maintenance and rescue use to Par and HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone and to HCP via an online dashboard.

Reporting group title	Cohort 4: Data on maintenance and rescue use supplied to Par

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Information from sensors attached to Relvar/Breo ELLIPTA and salbutamol MDI was fed back to the participant via an application on smart phone.

Reporting group title	Cohort 5: No data supplied to Par or HCP

Reporting group description:

Eligible participants received Relvar/Breo maintenance therapy at doses of 100/25 mcg or 200/25 mcg per actuation administered via ELLIPTA DPI, one inhalation once daily. Participants also received salbutamol rescue medication at dose of 100 mcg per actuation administered via MDI, as and when required. Sensors were attached to both the inhalers to electronically record actuation data. Participants were provided with a home hub through which their data was uploaded during the study but the participants and their HCP were not able to view the data.

Serious adverse events	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 87 (2.30%)	1 / 88 (1.14%)	2 / 88 (2.27%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian germ cell teratoma			
subjects affected / exposed	0 / 87 (0.00%)	1 / 88 (1.14%)	0 / 88 (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
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	1 / 88 (1.14%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1

deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Obstructive pancreatitis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (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
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (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	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (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
Cellulitis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 4: Data on maintenance and rescue use supplied to Par	Cohort 5: No data supplied to Par or HCP	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 88 (1.14%)	4 / 86 (4.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian germ cell teratoma			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	

deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Obstructive pancreatitis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
pneumonia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Cohort 1: Data on maintenance use supplied to Par and HCP	Cohort 2: Data on maintenance use supplied to Par	Cohort 3: Data on maintenance and rescue use to Par and HCP
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 87 (4.60%)	1 / 88 (1.14%)	1 / 88 (1.14%)
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 87 (1.15%)	1 / 88 (1.14%)	0 / 88 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 87 (0.00%)	1 / 88 (1.14%)	0 / 88 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 87 (0.00%)	1 / 88 (1.14%)	0 / 88 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
fatigue			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 87 (0.00%)	1 / 88 (1.14%)	0 / 88 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0

Arthralgia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Oral Candidiasis			
subjects affected / exposed	2 / 87 (2.30%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	2	0	0
Oesophageal candidiasis			
subjects affected / exposed	1 / 87 (1.15%)	0 / 88 (0.00%)	0 / 88 (0.00%)
occurrences (all)	1	0	0
Oral fungal infection			
subjects affected / exposed	0 / 87 (0.00%)	1 / 88 (1.14%)	0 / 88 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 88 (0.00%)	1 / 88 (1.14%)
occurrences (all)	0	0	1

Non-serious adverse events	Cohort 4: Data on maintenance and rescue use supplied to Par	Cohort 5: No data supplied to Par or HCP	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 88 (1.14%)	2 / 86 (2.33%)	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
Dysgeusia			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			

fatigue			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 88 (0.00%)	1 / 86 (1.16%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 86 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	1 / 88 (1.14%)	1 / 86 (1.16%)	
occurrences (all)	1	1	
Infections and infestations			
Oral Candidiasis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
Oral fungal infection			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 88 (0.00%)	0 / 86 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2018	Amendment 01: Sections: synopsis, overall design, number of participants, scientific rationale for study design and method of treatment assignment were modified - sample size re-estimation and interim analysis were deleted. Updated schedule of activities-requirement to collect protocol defined safety events from start of run-in and once a participant has begun treatment with Relvar/Breo added to table and notes. Updated the section: benefit/risk assessment to remove potential risks to align with the latest risk management plan (RMP). Updated objectives and endpoints to delete prescriptions filled from healthcare utilization endpoints, to add asthma control test (ACT) composite endpoint, correction to asthma symptom utility index (ASUI) endpoint and correction to beliefs in medicine questionnaire (BMQ) endpoint. Section: overall design modified to clarify early withdrawal. Text amended in concomitant therapy, discontinuation criteria, BMQ, exit interviews, asthma exacerbations, biomarkers and prescription record for asthma maintenance medication.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

 None reported