Clinical trial results:
An escalating dose, randomized, placebo-controlled incomplete block, 2-period cross-over study to assess the dose response for topical efficacy via airway responsiveness to adenosine-5'-monophosphate (AMP) challenge and the dose response for systemic activity via 24h plasma cortisol suppression and thereby the relative therapeutic index for fluticasone furoate (FF), fluticasone propionate (FP) and budesonide (BUD) in asthmatic participants.

Summary

EudraCT number	2016-003002-14
Trial protocol	GB DE
Global end of trial date	20 December 2018

Results information

Result version number	v1 (current)
This version publication date	19 February 2020
First version publication date	19 February 2020

Trial information

Trial identification

Sponsor protocol code	203162

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, 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	23 April 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the dose response and relative potency for increasing doses of Fluticasone Furoate (FF), Fluticasone Propionate (FP) and Budesonide (BUD) in the adenosine monophosphate (AMP) challenge model at 12 hours after the last dose on Day 7. - To assess the dose response and relative potency for FF, FP and BUD on 24 hour plasma cortisol suppression on treatment from pre-dose PM dose on Day 6 to pre-dose PM dose Day 7 - To assess the therapeutic index for FF, FP and BUD.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 46
Country: Number of subjects enrolled	Germany: 10
Worldwide total number of subjects	56
EEA total number of subjects	56

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)	55
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 56 participants were enrolled across 1 center in Germany and 2 centers in the United Kingdom.

Pre-assignment

Screening details:

A total of 165 participants were screened of which 109 failed screening and 56 participants were enrolled in the study. Of the 56 participants enrolled, only 54 were randomized and received at least one dose of study medication.

Period 1

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

Arms

Arm title	Total

Arm description:

Participants received Fluticasone Furoate (FF) Fluticasone Propionate, Budesonide (BUD), Placebo via inhalers ELLIPTA and DISKUS as morning (AM) and evening (PM) dose for treatment Period 1 and treatment period 2 of the study period. Washout was be a minimum of 25 days to maximum of 42 days between the two treatment periods.

Arm type	Experimental
Investigational medicinal product name	Fluticasone Propionate (FP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Dry Inhalation powder 50 mcg, 100 mcg, 250 mcg, and 500 mcg per blister strip was administered using DISKUS dry powder inhaler (DPI) in both treatment periods.

Investigational medicinal product name	Fluticasone Furoate (FF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Dry inhalation powder 25 mcg, 100 mcg, and 200 mcg per blister strip was administered using ELLIPTA dry powder inhaler (DPI) in both treatment periods.

Investigational medicinal product name	Budesonide (BUD)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Budesonide was available as white to off-white rounded granules, which disintegrated to a fine powder upon slight pressure and was administered using Turbuhaler in both treatment periods.

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 dry powder was administered using ELLIPTA or DISKUS in both treatment periods.

Number of subjects in period 1[1]	Total
Started	54
Completed	45
Not completed	9
Consent withdrawn by subject	7
Poor Spirometry efforts	1
Lost to follow-up	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Of the 56 participants enrolled, only 54 were randomized and received at least one dose of study medication.

Baseline characteristics

Reporting groups

Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	54	54	
Age Categorical Units: Participants			
Total Participants	54	54	
Age continuous Units: years			
arithmetic mean	37.9		
standard deviation	± 13.96	-	
Sex: Female, Male Units: Participants			
Female	13	13	
Male	41	41	
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE	1	1	
BLACK OR AFRICAN AMERICAN	7	7	
WHITE - ARABIC/NORTH AFRICAN HERITAGE	1	1	
MULTIPLE	2	2	
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE	39	39	
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	4	4	

Subject analysis sets

Subject analysis set title	All Participants
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants in this arm received FF, FP, BUD and Placebo during the study period.

Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.

Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	
Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.	

Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	Fluticasone Furoate (FF)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg for 7 days.	
Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.	
Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.	
Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.	
Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.	
Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 2 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 4 puff PM as total daily dose for 7 days	
Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 400 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mcg 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mcg 1 puff PM as total daily dose for 7 days	

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 250 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 250 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 500 mcg 2 puffs AM and 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP DISKUS 500 mcg 2 puffs AM and 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	

Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	
Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	
Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.	
Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.	
Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.	

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	
Subject analysis set title	Fluticasone furoate (FF)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.	
Subject analysis set title	Fluticasone Furoate (FF)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.	
Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.	
Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	Fluticasone furoate (FF)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Reporting group values	All Participants	FF 25 mcg	FF 100 mcg
Number of subjects	54	19	19
Age Categorical Units: Participants			
Total Participants	54	19	19
Age continuous Units: years			
arithmetic mean	37.9		
standard deviation	± 13.96	±	±
Sex: Female, Male Units: Participants			
Female	13		
Male	41		

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE	1		
BLACK OR AFRICAN AMERICAN	7		
WHITE - ARABIC/NORTH AFRICAN HERITAGE	1		
MULTIPLE	2		
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE	39		
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE	4		

Reporting group values	FF 200 mcg	FF 400 mcg	FF 800 mcg
Number of subjects	18	18	17
Age Categorical Units: Participants			
Total Participants	18	18	17
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female			
Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE			
BLACK OR AFRICAN AMERICAN			
WHITE - ARABIC/NORTH AFRICAN HERITAGE			
MULTIPLE			
WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE			
ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 50 mcg	FP 200 mcg	FP 500 mcg
Number of subjects	20	20	18
Age Categorical Units: Participants			
Total Participants	20	20	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female			
Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 1000 mcg	FP 2000 mcg	BUD 100 mcg
Number of subjects	16	17	18
Age Categorical Units: Participants			
Total Participants	16	17	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Number of subjects	18	18	18
Age Categorical Units: Participants			
Total Participants	18	18	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 3200 mcg	FF 800 mcg	FP 2000 mcg
Number of subjects	17	18	16
Age Categorical Units: Participants			
Total Participants	17	18	16
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 100 mcg	BUD 400 mcg	Fluticasone Furoate (FF)
Number of subjects	16	16	51
Age Categorical Units: Participants			
Total Participants	16	16	51
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Fluticasone Propionate (FP)	FP 200 mcg	Placebo
Number of subjects	51	19	17
Age Categorical Units: Participants			
Total Participants	51	19	17
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 25 mcg	FF 200 mcg	FP 50 mcg
Number of subjects	20	19	21
Age Categorical Units: Participants			
Total Participants	20	19	21
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Number of subjects	20	18	18
Age Categorical Units: Participants			
Total Participants	20	18	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Placebo	Placebo	FF 25 mcg
Number of subjects	12	4	14
Age Categorical Units: Participants			
Total Participants	12	4	14
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 25 mcg	FF 100 mcg	FF 100 mcg
Number of subjects	6	13	6
Age Categorical Units: Participants			
Total Participants	6	13	6
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 200 mcg	FF 200 mcg	FF 400 mcg
Number of subjects	13	6	12
Age Categorical Units: Participants			
Total Participants	13	6	12
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 800 mcg	FF 400 mcg	FP 50 mcg
Number of subjects	12	6	15
Age Categorical Units: Participants			
Total Participants	12	6	15
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 50 mcg	FP 200 mcg	FP 200 mcg
Number of subjects	6	14	6
Age Categorical Units: Participants			
Total Participants	6	14	6
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 500 mcg	FP 500 mcg	FP 1000 mcg
Number of subjects	14	6	11
Age Categorical Units: Participants			
Total Participants	14	6	11
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 1000 mcg	FP 2000 mcg	FP 2000 mcg
Number of subjects	6	10	6
Age Categorical Units: Participants			
Total Participants	6	10	6
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 100 mcg	BUD 100 mcg	BUD 400 mcg
Number of subjects	12	4	12
Age Categorical Units: Participants			
Total Participants	12	4	12
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 400 mcg	BUD 800 mcg	BUD 800 mcg
Number of subjects	5	11	5
Age Categorical Units: Participants			
Total Participants	5	11	5
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 1600 mcg	BUD 1600 mcg	BUD 3200 mcg
Number of subjects	11	5	10
Age Categorical Units: Participants			
Total Participants	11	5	10
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 3200 mcg	FF 400 mcg	Placebo
Number of subjects	5	19	17
Age Categorical Units: Participants			
Total Participants	5	19	17
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 25 mcg	FF 100 mcg	FF 200 mcg
Number of subjects	20	19	19
Age Categorical Units: Participants			
Total Participants	20	19	19
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FF 400 mcg	FF 800 mcg	FP 50 mcg
Number of subjects	18	18	21
Age Categorical Units: Participants			
Total Participants	18	18	21
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 200 mcg	FP 500 mcg	FP 1000 mcg
Number of subjects	20	20	18
Age Categorical Units: Participants			
Total Participants	20	20	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	FP 2000 mcg	BUD 100 mcg	BUD 400 mcg
Number of subjects	17	18	18
Age Categorical Units: Participants			
Total Participants	17	18	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	BUD 800 mcg	BUD 1600 mcg	BUD 3200 mcg
Number of subjects	18	18	18
Age Categorical Units: Participants			
Total Participants	18	18	18
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Fluticasone furoate (FF)	Fluticasone Furoate (FF)	Budesonide (BUD)
Number of subjects	14	15	12
Age Categorical Units: Participants			
Total Participants	14	15	12
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Placebo	Fluticasone furoate (FF)	Fluticasone Propionate (FP)
Number of subjects	5	6	6
Age Categorical Units: Participants			
Total Participants	5	6	6
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Budesonide (BUD)	Fluticasone Propionate (FP)	Budesonide (BUD)
Number of subjects	6	5	6
Age Categorical Units: Participants			
Total Participants	6	5	6
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			

Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

Reporting group values	Fluticasone Propionate (FP)	Budesonide (BUD)	Budesonide (BUD)
Number of subjects	6	6	51
Age Categorical Units: Participants			
Total Participants	6	6	
Age continuous Units: years arithmetic mean standard deviation	±	±	±
Sex: Female, Male Units: Participants			
Female Male			
Race/Ethnicity, Customized Units: Subjects			
ASIAN - EAST ASIAN HERITAGE BLACK OR AFRICAN AMERICAN WHITE - ARABIC/NORTH AFRICAN HERITAGE MULTIPLE WHITE - WHITE/CAUCASIAN/EUROPEAN HERITAGE ASIAN - CENTRAL/SOUTH ASIAN HERITAGE			

End points

End points reporting groups

Reporting group title	Total
Reporting group description:	
Participants received Fluticasone Furoate (FF) Fluticasone Propionate, Budesonide (BUD), Placebo via inhalers ELLIPTA and DISKUS as morning (AM) and evening (PM) dose for treatment Period 1 and treatment period 2 of the study period. Washout was be a minimum of 25 days to maximum of 42 days between the two treatment periods.	
Subject analysis set title	All Participants
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants in this arm received FF, FP, BUD and Placebo during the study period.	
Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.	
Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.	
Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.

Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.

Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	Fluticasone Furoate (FF)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.

Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FF ELLIPTA 200 mcg 2 puff PM as total daily dose for 7 days

Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FF ELLIPTA 200 mcg 4 puff PM as total daily dose for 7 days

Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FF ELLIPTA 400 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP ELLIPTA 50 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP ELLIPTA 50 mcg 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 250 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 250 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days

Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:
Participants received FP DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP DISKUS 500 mcg 2 puffs AM and 2 puffs PM as total daily dose for 7 days.

Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP DISKUS 500 mcg 2 puffs AM and 2 puffs PM as total daily dose for 7 days.

Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.

Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.

Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	FF 25 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.

Subject analysis set title	FF 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FF 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.

Subject analysis set title	FF 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.

Subject analysis set title	FP 50 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 500 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 1000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	FP 2000 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 100 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 400 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 800 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 1600 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Subject analysis set title	BUD 3200 mcg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.

Subject analysis set title	Fluticasone furoate (FF)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.

Subject analysis set title	Fluticasone Furoate (FF)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Placebo
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Subject analysis set title	Fluticasone furoate (FF)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FF ELLIPTA 25 mcg, 100 mcg, 200 mcg, 400 mcg, 800 mcg PM as total daily dose for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Fluticasone Propionate (FP)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.

Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.	
Subject analysis set title	Budesonide (BUD)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received FP ELLIPTA 50 mg, 200 mcg, 500 mcg, 1000 mcg, 2000 mcg for 7 days.	

Primary: Provocative concentration (PC) of adenosine 5' monophosphate (AMP) causing a 20 percent (%) reduction in forced expiratory volume in 1 second (FEV1) (AMP PC20)

End point title	Provocative concentration (PC) of adenosine 5' monophosphate (AMP) causing a 20 percent (%) reduction in forced expiratory volume in 1 second (FEV1) (AMP PC20)

End point description:

The percentage fall in FEV1 was calculated using highest FEV1 (post saline) minus highest FEV1 (post AMP) divided by highest FEV1 (post saline)*100 where highest FEV1 (post saline) is the highest value of two FEV1 measurements at 60 and 180 seconds after the saline control, highest FEV1 (post AMP) is the highest value of the two FEV1 measurements at 60 and 180 seconds after the dose of AMP. Results are presented treatment wise. Pharmacodymanic (PD) population comprised of participants who were randomized and received at least one post dose of PD measurement. Only those participants with data available at the specified time points were analyzed. Mean and 95% Confidence Interval (CI) presented are predicted estimate.

End point type	Primary

End point timeframe:

12 hours post last dose on Day 7

End point values	FF 25 mcg	FF 100 mcg	FF 200 mcg	FF 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[1]	19[2]	18[3]	18[4]
Units: Milligrams per milliliter				
arithmetic mean (confidence interval 95%)	33.45 (19.10 to 58.60)	81.45 (44.65 to 148.58)	115.69 (66.82 to 200.31)	145.97 (85.02 to 250.59)

Notes:

[1] - Pharmacodynamic (PD) Population.

[2] - PD Population.

[3] - PD Population.

[4] - PD Population.

End point values	FF 800 mcg	FP 50 mcg	FP 200 mcg	FP 500 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	17[5]	20[6]	20[7]	18[8]
Units: Milligrams per milliliter				
arithmetic mean (confidence interval 95%)	167.26 (95.36 to 293.37)	15.19 (10.80 to 21.36)	20.47 (13.94 to 30.07)	31.39 (18.88 to 52.19)

Notes:

[5] - PD Population.

[6] - PD Population.

[7] - PD Population.

[8] - PD Population.

End point values	FP 1000 mcg	FP 2000 mcg	BUD 100 mcg	BUD 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	16[9]	17[10]	18[11]	18[12]
Units: Milligrams per milliliter				
arithmetic mean (confidence interval 95%)	48.67 (27.30 to 86.78)	76.35 (43.21 to 134.91)	16.00 (11.41 to 22.44)	23.91 (15.08 to 37.90)

Notes:

[9] - PD Population.

[10] - PD Population.

[11] - PD Population.

[12] - PD Population.

End point values	BUD 800 mcg	BUD 1600 mcg	BUD 3200 mcg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	18[13]	18[14]	17[15]	
Units: Milligrams per milliliter				
arithmetic mean (confidence interval 95%)	34.62 (19.28 to 62.16)	54.33 (28.40 to 103.93)	84.17 (45.48 to 155.79)	

Notes:

[13] - PD Population.

[14] - PD Population.

[15] - PD Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	FF 25 mcg v FF 200 mcg v FF 400 mcg v FF 800 mcg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.39
upper limit	19.39

Statistical analysis title	Statistical Analysis 2
Comparison groups	FF 25 mcg v FF 200 mcg v FF 400 mcg v FF 800 mcg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	14.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.21
upper limit	25.4

Statistical analysis title	Statistical Analysis 3
Comparison groups	FF 25 mcg v FF 200 mcg v FF 400 mcg v FF 800 mcg
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	48.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.21
upper limit	129.32

Statistical analysis title	Statistical Analysis 4
Comparison groups	FP 50 mcg v FP 200 mcg v FP 500 mcg v FP 1000 mcg v FP 2000 mcg
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.39
upper limit	19.39

Statistical analysis title	Statistical Analysis 5
Comparison groups	FP 50 mcg v FP 200 mcg v FP 500 mcg v FP 1000 mcg v FP 2000 mcg
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	14.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.21
upper limit	25.4

Statistical analysis title	Statistical Analysis 6
Comparison groups	FP 50 mcg v FP 200 mcg v FP 500 mcg v FP 1000 mcg v FP 2000 mcg
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	1081.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	448
upper limit	2609.66

Statistical analysis title	Statistical Analysis 7
Comparison groups	BUD 100 mcg v BUD 400 mcg v BUD 800 mcg v BUD 1600 mcg v BUD 3200 mcg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.39
upper limit	19.39

Statistical analysis title	Statistical Analysis 8
Comparison groups	BUD 100 mcg v BUD 400 mcg v BUD 800 mcg v BUD 1600 mcg v BUD 3200 mcg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	14.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.21
upper limit	25.4

Statistical analysis title	Statistical Analysis 9
Comparison groups	BUD 100 mcg v BUD 400 mcg v BUD 800 mcg v BUD 1600 mcg v BUD 3200 mcg

Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	3 parameter Emax model
Point estimate	1467.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	546.51
upper limit	3939.84

Primary: Cortisol Suppression 0-24 Hours Weighted Mean

End point title	Cortisol Suppression 0-24 Hours Weighted Mean

End point description:

Blood samples for measurement of plasma cortisol were collected at given time point. The weighted means were derived by calculating the area under the curve (AUC) over the 0-24-hour period using the trapezoidal rule, and then dividing it by the actual time interval. Results are presented treatment wise. Only those participants with data available at the specified time points were analyzed. Mean and 95% Confidence Interval (CI) presented are predicted estimate.

End point type	Primary

End point timeframe:

Pre-dose PM dose on Day 6 to pre-dose PM dose Day 7

End point values	FF 25 mcg	FF 100 mcg	FF 200 mcg	FF 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[16]	19[17]	18[18]	18[19]
Units: nanomoles per liter				
arithmetic mean (confidence interval 95%)	172.73 (159.88 to 186.62)	163.03 (151.01 to 176.02)	150.95 (139.48 to 163.37)	129.40 (117.82 to 142.12)

Notes:

[16] - PD Population.

[17] - PD Population.

[18] - PD Population.

[19] - PD Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 800 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	20[20]	18[21]	16[22]	18[23]
Units: nanomoles per liter				
arithmetic mean (confidence interval 95%)	173.04 (160.15 to 186.97)	147.89 (136.59 to 160.13)	124.21 (112.88 to 136.68)	132.06 (122.05 to 142.90)

Notes:

[20] - PD Population.

[21] - PD Population.

[22] - PD Population.

[23] - PD Population.

End point values	BUD 1600 mcg	BUD 3200 mcg	FF 800 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[24]	17[25]	18[26]	16[27]
Units: nanomoles per liter				
arithmetic mean (confidence interval 95%)	99.05 (90.24 to 108.72)	55.71 (48.26 to 64.31)	95.09 (82.26 to 109.93)	87.62 (75.37 to 101.85)

Notes:

[24] - PD Population.

[25] - PD Population.

[26] - PD Population.

[27] - PD Population.

End point values	BUD 100 mcg	BUD 400 mcg	FP 200 mcg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16[28]	16[29]	19[30]	
Units: nanomoles per liter				
arithmetic mean (confidence interval 95%)	169.87 (157.23 to 183.52)	152.50 (141.26 to 164.63)	164.22 (152.11 to 177.29)	

Notes:

[28] - PD Population.

[29] - PD Population.

[30] - PD Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	FF 25 mcg v FF 100 mcg v FF 200 mcg v FF 400 mcg
Number of subjects included in analysis	74
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Exponential power-law model
Point estimate	176.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	162.87
upper limit	190.38

Statistical analysis title	Statistical Analysis 2
Comparison groups	FF 25 mcg v FF 100 mcg v FF 200 mcg v FF 400 mcg v FF 800 mcg

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	exponential power-law model
Point estimate	899.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	698.36
upper limit	1101.62

Statistical analysis title	Statistical Analysis 3
Comparison groups	FP 50 mcg v FP 200 mcg v FP 500 mcg v FP 1000 mcg v FP 2000 mcg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	exponential power-law model
Point estimate	176.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	162.87
upper limit	190.38

Statistical analysis title	Statistical Analysis 4
Comparison groups	FP 50 mcg v FP 200 mcg v FP 500 mcg v FP 1000 mcg v FP 2000 mcg
Number of subjects included in analysis	89
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	exponential power-law model
Point estimate	1986.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	1574.7
upper limit	2397.39

Statistical analysis title	Statistical Analysis 5
Comparison groups	BUD 100 mcg v BUD 400 mcg v BUD 800 mcg v BUD 1600 mcg

Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	exponential power-law model
Point estimate	176.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	162.87
upper limit	190.38

Statistical analysis title	Statistical Analysis 6
Comparison groups	BUD 100 mcg v BUD 400 mcg v BUD 800 mcg v BUD 1600 mcg v BUD 3200 mcg
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	exponential power-law model
Point estimate	1927.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	1698.47
upper limit	2156.37

Primary: Theraputic index of FF

End point title	Theraputic index of FF[31]

End point description:

Therapeutic Index was calculated by ED20 for Cortisol Suppression 0-24 Hours Weighted Mean (nanomoles per liter[nmol/L]) divided by Dose at which 80% of the maximum effect is reached (ED80) for AMP PC20 for FF 25 mcg, FF 100 mcg, FF 200 mcg, FF 400 mcg, FF 800 mcg. Theraputic index has been presented. Only those participants with data available at the specified time points were analyzed. The timeframe mentioned is for AMP PC20 and Cortisol suppression respectively. The Estimate for ED20 Cortisol Suppression is 289.73 along with 95% CI (224.82, 354.64), the estimate for ED80 AMP PC20 is 194.09 along with 95% CI (72.82, 517.28).

End point type	Primary

End point timeframe:

12 hours post-dose on Day 7, pre-dose PM dose on Day 6 to pre-dose PM dose Day 7

Notes:

[31] - 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: The Statistical Analysis for this endpoint is presented in the Outcomes measure description.

End point values	Fluticasone Furoate (FF)			
Subject group type	Subject analysis set			
Number of subjects analysed	51[32]			
Units: Ratio				
number (not applicable)	1.49			

Notes:

[32] - PD Population.

Statistical analyses

No statistical analyses for this end point

Primary: Theraputic index of FP

End point title	Theraputic index of FP[33]

End point description:

Therapeutic Index was calculated by Dose at which 20% of the maximum effect is reached (ED20) for Cortisol Suppression 0-24 Hours Weighted Mean (nanomoles per liter[nmol/L]) divided by ED80 for AMP PC20 for FP 50 mcg, FP 200 mcg, FP 500 mcg, FP 1000 mcg, FP 2000 mcg. Theraputic index has been presented. Only those participants with data available at the specified time points were analyzed. The timeframe mentioned is for AMP PC20 and Cortisol suppression respectively. The Estimate for ED20 Cortisol Suppression is 639.36 along with 95% CI (506.94, 771.79), the estimate for ED80 AMP PC20 is 4325.07 along with 95% CI (1792.02, 10438.64).

End point type	Primary

End point timeframe:

12 hours post-dose on Day 7, pre-dose PM dose on Day 6 to pre-dose PM dose Day 7

Notes:

[33] - 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: The Statistical Analysis for this endpoint is presented in the Outcomes measure description.

End point values	Fluticasone Propionate (FP)			
Subject group type	Subject analysis set			
Number of subjects analysed	51[34]			
Units: Ratio				
number (not applicable)	0.15			

Notes:

[34] - PD Population.

Statistical analyses

No statistical analyses for this end point

Primary: Theraputic index of BUD

End point title	Theraputic index of BUD[35]

End point description:

Therapeutic Index was calculated by ED20 for Cortisol Suppression 0-24 Hours Weighted Mean (nanomoles per liter[nmol/L]) divided by ED80 for AMP PC20 for BUD 100 mcg, BUD 400 mcg, BUD 800 mcg, BUD 1600 mcg, BUD 3200 mcg. Theraputic index has been presented. Only those participants with data available at the specified time points were analyzed. The timeframe mentioned is for AMP PC20 and Cortisol suppression respectively. The Estimate for ED20 Cortisol Suppression is 620.49 along with 95% CI (546.79, 694.20), the estimate for ED80 AMP PC20 is 5869.45 along with 95% CI (2186.03, 15759.35).

End point type	Primary

End point timeframe:

12 hours post-dose on Day 7, pre-dose PM dose on Day 6 to pre-dose PM dose Day 7

Notes:

[35] - 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: The Statistical Analysis for this endpoint is presented in the Outcomes measure description.

End point values	Budesonide (BUD)			
Subject group type	Subject analysis set			
Number of subjects analysed	51[36]			
Units: Ratio				
number (not applicable)	0.11			

Notes:

[36] - PD Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) and any serious adverse event (SAE)

End point title	Number of participants with any adverse event (AE) and any serious adverse event (SAE)

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. SAE is any untoward medical occurrence that at any dose results in death, Is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect. Results are presented treatment wise. All Subjects Population will consist of all participants who were randomized and who received at least one dose of trial medication.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FF 400 mcg	FP 200 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[37]	18[38]	20[39]	17[40]
Units: Participants				
Any AEs	8	6	4	6
Any SAEs	0	0	0	0

Notes:

[37] - All Subjects Population.

[38] - All Subjects Population.

[39] - All Subjects Population.

[40] - All Subjects Population.

End point values	BUD 100 mcg	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[41]	18[42]	18[43]	18[44]

Units: Participants				
Any AEs	6	8	5	6
Any SAEs	0	0	0	0

Notes:

[41] - All Subjects Population.

[42] - All Subjects Population.

[43] - All Subjects Population.

[44] - All Subjects Population.

End point values	FF 800 mcg	Placebo	FF 25 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[45]	17[46]	20[47]	19[48]
Units: Participants				
Any AEs	7	10	6	7
Any SAEs	0	0	0	0

Notes:

[45] - All Subjects Population.

[46] - All Subjects Population.

[47] - All Subjects Population.

[48] - All Subjects Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21[49]	20[50]	18[51]	18[52]
Units: Participants				
Any AEs	10	4	8	3
Any SAEs	0	0	0	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: Peak expiratory flow rate (PEFR) as a measure of safety and tolerability of Placebo in Period 1

End point title	Peak expiratory flow rate (PEFR) as a measure of safety and tolerability of Placebo in Period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Participants recorded their PEFR measurement before each dose in a paper diary. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Day 2 to 8 PM, Day 9 to 14 AM and PM, Day 15 PM, Day 16 to 21 AM and PM, Day 22 PM, Day 23 to 28 AM and PM, Day 29 PM, Day 30 to 35 AM and PM in period 1

End point values	Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2, PM, n=12	522.5 (± 25.4)			
Day 3, PM, n=12	517.5 (± 27.0)			
Day 4, PM, n=12	514.2 (± 27.8)			
Day 5,PM, n=12	521.7 (± 24.2)			
Day 6, PM, n=12	522.5 (± 29.1)			
Day 7, PM, n=12	539.2 (± 32.3)			
Day 8, PM, n=12	530.8 (± 27.8)			
Day 9, AM, n=5	576.0 (± 37.5)			
Day 9, PM, n=12	531.3 (± 27.9)			
Day 10, AM, n=5	572.0 (± 34.4)			
Day 10, PM, n=12	535.0 (± 22.0)			
Day 11, AM, n=5	578.0 (± 35.9)			
Day 11, PM, n=12	533.8 (± 29.0)			
Day 12, AM, n=5	578.0 (± 37.2)			
Day 12 PM, n=12	527.5 (± 26.7)			
Day 13, AM, n=5	580.0 (± 37.4)			
Day 13, PM, n=12	540.8 (± 25.1)			
Day 14, AM, n=5	572.0 (± 34.7)			
Day 14, PM, n=12	543.3 (± 26.4)			
Day 15, PM, n=12	530.8 (± 26.0)			
Day 16, AM, n=5	588.0 (± 36.1)			
Day 16,PM, n=12	528.3 (± 24.4)			
Day 17, AM, n=5	586.0 (± 31.7)			
Day 17,PM, n=12	521.7 (± 32.5)			
Day 18, AM, n=5	586.0 (± 35.0)			
Day 18,PM, n=12	540.0 (± 26.9)			
Day 19, AM, n=5	568.0 (± 38.3)			
Day 19,PM, n=12	535.8 (± 29.3)			
Day 20, AM, n=5	596.0 (± 37.5)			
Day 20,PM, n=12	544.2 (± 28.2)			
Day 21, AM, n=5	580.0 (± 31.4)			
Day 21,PM, n=12	534.2 (± 32.6)			
Day 22,PM, n=11	544.5 (± 29.0)			
Day 23, AM, n=4	577.5 (± 37.9)			
Day 23,PM, n=11	530.0 (± 27.4)			
Day 24, AM, n=4	567.5 (± 39.4)			
Day 24,PM, n=11	526.4 (± 26.5)			
Day 25, AM, n=4	585.0 (± 39.2)			
Day 25,PM, n=11	530.9 (± 29.6)			
Day 26, AM, n=4	582.5 (± 40.0)			
Day 26,PM, n=11	518.2 (± 30.0)			
Day 27, AM, n=4	587.5 (± 40.0)			
Day 27,PM, n=11	539.1 (± 29.3)			

Day 28, AM, n=4	587.5 (± 43.0)			
Day 28,PM, n=10	547.0 (± 30.4)			
Day 29,PM, n=11	547.3 (± 28.2)			
Day 30, AM, n=4	567.5 (± 38.1)			
Day 30,PM, n=11	527.3 (± 26.6)			
Day 31, AM, n=4	562.5 (± 33.2)			
Day 31,PM, n=11	537.3 (± 26.5)			
Day 32, AM, n=4	582.5 (± 40.2)			
Day 32,PM, n=11	537.3 (± 26.2)			
Day 33, AM, n=4	597.5 (± 40.0)			
Day 33,PM, n=11	528.2 (± 30.5)			
Day 34, AM, n=4	580.0 (± 39.3)			
Day 34,PM, n=11	531.4 (± 31.9)			
Day 35, AM, n=4	565.0 (± 38.8)			
Day 35,PM, n=11	501.8 (± 26.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability of Placebo in Period 2

End point title	PEFR as a measure of safety and tolerability of Placebo in Period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Participants recorded their PEFR measurement before each dose in a paper diary. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed (represented by n=X in the category titles). 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Day 2 to 8 PM, Day 9 to 14 AM and PM, Day 15 PM, Day 16 to 21 AM and PM, Day 22 PM, Day 23 to 28 AM and PM, Day 29 PM, Day 30 to 35 AM and PM in Period 2

End point values	Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	4[53]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2, PM, n=4	422.5 (± 28.9)			
Day 3, PM, n=4	415.0 (± 27.2)			
Day 4, PM, n=4	398.8 (± 26.6)			
Day 5,PM, n=4	407.5 (± 37.5)			
Day 6, PM, n=4	411.3 (± 29.0)			
Day 7, PM, n=4	410.0 (± 36.7)			
Day 8, PM, n=4	415.0 (± 36.1)			
Day 9, AM, n=2	430.0 (± 80.0)			
Day 9, PM, n=4	411.3 (± 45.4)			

Day 10, AM, n=2	425.0 (± 65.0)			
Day 10, PM, n=4	403.8 (± 37.1)			
Day 11, AM, n=2	410.0 (± 60.0)			
Day 11, PM, n=4	395.0 (± 29.0)			
Day 12, AM, n=2	400.0 (± 50.0)			
Day 12, PM, n=4	398.8 (± 28.6)			
Day 13, AM, n=2	415.0 (± 95.0)			
Day 13, PM, n=4	425.0 (± 35.2)			
Day 14, AM, n=2	425.0 (± 65.0)			
Day 14, PM, n=3	420.0 (± 40.4)			
Day 15, PM, n=4	416.3 (± 37.0)			
Day 16, AM, n=2	405.0 (± 75.0)			
Day 16, PM, n=4	405.0 (± 32.0)			
Day 17, AM, n=2	390.0 (± 70.0)			
Day 17, PM, n=4	405.0 (± 28.9)			
Day 18, AM, n=1	450.0 (± 99999)			
Day 18, PM,n=3	423.3 (± 34.8)			
Day 19, AM, n=2	415.0 (± 65.0)			
Day 19, PM, n=4	402.5 (± 30.1)			
Day 20, AM, n=2	402.5 (± 57.5)			
Day 20, PM, n=4	398.8 (± 36.3)			
Day 21, AM, n=2	400.0 (± 60.0)			
Day 21,PM, n=4	395.0 (± 38.6)			
Day 22, PM, n=4	397.5 (± 34.9)			
Day 23, AM, n=1	480.0 (± 99999)			
Day 23, PM, n=3	415.0 (± 39.0)			
Day 24, AM, n=1	460.0 (± 99999)			
Day 24, PM, n=3	423.3 (± 38.4)			
Day 25, AM, n=1	460.0 (± 99999)			
Day 25, PM, n=3	416.7 (± 33.8)			
Day 26, AM, n=1	450.0 (± 99999)			
Day 26, PM, n=3	418.3 (± 36.7)			
Day 27, AM, n=1	460.0 (± 99999)			
Day 27,PM, n=3	433.3 (± 49.7)			
Day 28, AM, n=1	460.0 (± 99999)			
Day 28, PM, n=3	430.0 (± 49.3)			
Day 29, PM, n=3	380.0 (± 75.5)			
Day 30, AM, n=1	460.0 (± 99999)			
Day 30, PM, n=3	388.3 (± 78.0)			
Day 31, AM, n=1	480.0 (± 99999)			
Day 31, PM, n=3	390.0 (± 85.0)			
Day 32, AM, n=1	500.0 (± 99999)			
Day 32, PM, n=3	370.0 (± 73.7)			
Day 33, AM, n=1	470.0 (± 99999)			

Day 33, PM, n=3	370.0 (± 70.9)			
Day 34, AM, n=1	460.0 (± 99999)			
Day 34, PM, n=3	390.0 (± 83.2)			
Day 35, AM, n=1	480.0 (± 99999)			
Day 35, PM, n=2	345.0 (± 105.0)			

Notes:

[53] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 25 mcg in Period 1

End point title	PEFR as a measure of safety and tolerability for FF 25 mcg in Period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Days 2,3,4,5,6,7 PM in period 1

End point values	FF 25 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	14[54]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2, PM, n=14	479.6 (± 30.9)			
Day 3, PM, n=14	475.7 (± 32.9)			
Day 4, PM, n=14	473.0 (± 31.1)			
Day 5,PM, n=14	476.1 (± 26.6)			
Day 6, PM, n=13	503.1 (± 24.6)			
Day 7, PM, n=13	502.3 (± 28.1)			

Notes:

[54] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 25 mcg in Period 2

End point title	PEFR as a measure of safety and tolerability for FF 25 mcg in Period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the specified time

points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 2,3,4,5,6,7 PM in period 2

End point values	FF 25 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[55]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2, PM, n=5	572.0 (± 48.9)			
Day 3, PM, n=5	570.0 (± 54.5)			
Day 4, PM, n=5	568.0 (± 55.0)			
Day 5,PM, n=5	573.0 (± 54.9)			
Day 6, PM, n=6	550.8 (± 52.2)			
Day 7, PM, n=6	560.0 (± 45.3)			

Notes:

[55] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 100 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FF 100 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 8,9,10,11,12,13,14 PM in period 1

End point values	FF 100 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	13[56]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8, PM, n=13	497.3 (± 24.9)			
Day 9, PM, n=13	500.4 (± 28.2)			
Day 10, PM, n=13	491.2 (± 31.0)			
Day 11, PM, n=12	507.5 (± 30.9)			
Day 12, PM, n=13	500.2 (± 30.2)			
Day 13, PM, n=13	515.4 (± 29.7)			
Day 14, PM, n=13	505.8 (± 28.7)			

Notes:
[56] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 100 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FF 100 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Days 8,9,10,11,12,13,14 PM in period 2

End point values	FF 100 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[57]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8, PM	540.0 (± 43.8)			
Day 9, PM	567.5 (± 42.6)			
Day 10, PM	556.7 (± 43.4)			
Day 11, PM	561.7 (± 44.6)			
Day 12, PM	573.3 (± 50.0)			
Day 13, PM	563.3 (± 53.0)			
Day 14, PM	555.8 (± 46.9)			

Notes:
[57] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 200 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FF 200 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Day 15,16,17,18,19,20,21 PM in period 1

End point values	FF 200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	13[58]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15,PM, n=13	500.8 (± 30.8)			
Day 16,PM, n=13	500.0 (± 28.7)			
Day 17,PM, n=13	506.2 (± 29.8)			
Day 18,PM, n=13	514.2 (± 31.6)			
Day 19,PM, n=13	505.4 (± 29.0)			
Day 20,PM, n=12	505.8 (± 30.8)			
Day 21,PM, n=12	485.0 (± 28.2)			

Notes:

[58] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 200 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FF 200 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles). 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Days 15,16,17,18,19,20 PM, Day 21 AM and PM in period 2

End point values	FF 200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[59]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15,PM, n=6	575.0 (± 52.9)			
Day 16,PM, n=6	575.0 (± 48.1)			
Day 17,PM, n=6	564.2 (± 46.6)			
Day 18,PM, n=6	573.3 (± 56.6)			
Day 19,PM, n=6	556.7 (± 53.4)			
Day 20,PM, n=6	571.7 (± 50.0)			
Day 21,AM, n=1	670.0 (± 99999)			
Day 21,PM, n=6	560.0 (± 38.3)			

Notes:
[59] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 400 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FF 400 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 22,23,24,25,26,27,28 PM in period 1

End point values	FF 400 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	12[60]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM	496.7 (± 30.5)			
Day 23 PM	481.0 (± 25.6)			
Day 24 PM	484.6 (± 25.2)			
Day 25 PM	488.3 (± 26.2)			
Day 26 PM	496.7 (± 28.8)			
Day 27 PM	508.8 (± 28.9)			
Day 28 PM	486.7 (± 23.7)			

Notes:
[60] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 400 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FF 400 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the indicated time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 22,23,24,25,26,27,28 PM in period 2

End point values	FF 400 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	12[61]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM	556.7 (± 46.9)			
Day 23 PM	566.7 (± 47.8)			
Day 24 PM	571.7 (± 50.8)			
Day 25 PM	568.3 (± 52.7)			
Day 26 PM	565.0 (± 43.0)			
Day 27 PM	540.0 (± 43.3)			
Day 28 PM	541.7 (± 41.2)			

Notes:

[61] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 800 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FF 800 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Days 29,30,31,32,33,34,35 PM in period 1

End point values	FF 800 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	12[62]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM	496.7 (± 27.0)			
Day 30 PM	487.1 (± 25.9)			
Day 31 PM	488.3 (± 24.1)			
Day 32 PM	481.3 (± 25.8)			
Day 33 PM	481.5 (± 24.9)			
Day 34 PM	487.5 (± 28.7)			
Day 35 PM	471.0 (± 26.6)			

Notes:
[62] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FF 800 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FF 800 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Days 29,30,31,32,33,34,35 PM in period 2

End point values	FF 400 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[63]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM	576.7 (± 44.9)			
Day 30 PM	560.0 (± 48.7)			
Day 31 PM	553.3 (± 45.0)			
Day 32 PM	565.0 (± 50.7)			
Day 33 PM	580.0 (± 48.9)			
Day 34 PM	568.3 (± 42.3)			
Day 35 PM	556.7 (± 44.9)			

Notes:
[63] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 50 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FP 50 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at the specified time points were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Days 2,3,4,5,6,7 PM in period 1

End point values	FP 50 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	15[64]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2 PM, n=15	529.3 (± 28.0)			
Day 3 PM, n=14	533.6 (± 30.3)			
Day 4 PM, n=15	532.3 (± 30.8)			
Day 5 PM, n=15	524.0 (± 29.9)			
Day 6 PM, n=14	519.3 (± 26.4)			
Day 7 PM, n=14	502.9 (± 35.1)			

Notes:

[64] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 50 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FP 50 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed (represented by n=X in the category titles). 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Day 2,3,4,5,6,7 AM and PM in period 2

End point values	FP 50 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[65]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2 AM, n=1	600.0 (± 99999)			
Day 2 PM, n=6	490.0 (± 40.6)			
Day 3 AM, n=1	600.0 (± 99999)			
Day 3 PM, n=6	486.7 (± 42.3)			
Day 4 AM, n=1	590.0 (± 99999)			
Day 4 PM, n=6	491.7 (± 42.6)			
Day 5 AM, n=1	600.0 (± 99999)			

Day 5 PM, n=6	491.7 (± 44.6)			
Day 6 AM, n=1	600.0 (± 99999)			
Day 6 PM, n=6	490.0 (± 44.3)			
Day 7 AM, n=1	600.0 (± 99999)			
Day 7 PM, n=6	466.0 (± 48.9)			

Notes:

[65] - All subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 200 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FP 200 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed (represented by n=X in the category titles). 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Days 8,9,1,0,11,12,13,14 AM and PM in period 1

End point values	FP 200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	14[66]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8 AM, n=1	540.0 (± 99999)			
Day 8 PM, n=13	532.7 (± 33.2)			
Day 9 AM, n=11	500.9 (± 38.3)			
Day 9 PM, n=14	517.9 (± 26.8)			
Day 10 AM, n=10	521.0 (± 39.0)			
Day 10 PM, n=14	513.2 (± 28.5)			
Day 11 AM, n=11	476.4 (± 35.4)			
Day 11 PM, n=14	512.1 (± 30.0)			
Day 12 AM, n=11	506.8 (± 38.0)			
Day 12 PM, n=13	528.8 (± 34.3)			
Day 13 AM, n=11	500.0 (± 38.2)			
Day 13 PM, n=14	514.6 (± 31.1)			
Day 14 AM, n=13	496.2 (± 31.7)			
Day14 PM, n=13	522.7 (± 32.9)			

Notes:

[66] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 200 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FP 200 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed. 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Day 8,9,1,0,11,12,13,14 AM and PM in period 2

End point values	FP 200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[67]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8 AM, n=1	610.0 (± 99999)			
Day 8 PM, n=6	500.0 (± 43.2)			
Day 9 AM, n=5	506.0 (± 39.5)			
Day 9 PM, n=6	488.3 (± 43.7)			
Day 10 AM, n=4	515.0 (± 44.0)			
Day 10 PM, n=6	490.0 (± 47.1)			
Day 11 AM, n=5	504.0 (± 36.1)			
Day 11 PM, n=6	485.0 (± 42.6)			
Day 12 AM, n=5	508.0 (± 41.4)			
Day 12 PM, n=6	493.3 (± 42.8)			
Day 13 AM, n=5	500.0 (± 40.1)			
Day 13 PM, n=6	495.0 (± 45.8)			
Day 14 AM, n=5	438.0 (± 46.6)			
Day 14 PM, n=6	495.8 (± 48.8)			

Notes:

[67] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 500 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FP 500 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed. 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Day 15 PM, Day 16,17,18,19,20,21,22,23,24,25,26,27,28 AM and PM in period 1

End point values	FP 500 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	14[68]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15 PM, n=14	527.5 (± 29.7)			
Day 16 AM, n=13	503.8 (± 31.9)			
Day 16 PM, n=14	520.4 (± 29.5)			
Day 17 AM, n=13	510.0 (± 30.3)			
Day 17 PM, n=14	508.6 (± 31.2)			
Day 18 AM, n=12	497.5 (± 34.7)			
Day 18 PM, n=13	505.8 (± 28.5)			
Day 19 AM, n=12	505.8 (± 35.2)			
Day 19 PM, n=13	506.9 (± 29.5)			
Day 20 AM, n=11	518.2 (± 35.9)			
Day 20 PM, n=13	517.3 (± 30.4)			
Day 21 AM, n=13	501.9 (± 32.1)			
Day 21 PM, n=11	493.6 (± 30.0)			
Day 22 AM, n=1	520.0 (± 99999)			
Day 22 PM, n=1	540.0 (± 99999)			
Day 23 AM, n=1	530.0 (± 99999)			
Day 23 PM, n=1	550.0 (± 99999)			
Day 24 AM, n=1	530.0 (± 99999)			
Day 24 PM, n=1	540.0 (± 99999)			
Day 25 AM, n=1	510.0 (± 99999)			
Day 25 PM, n=1	500.0 (± 99999)			
Day 26 AM, n=1	520.0 (± 99999)			
Day 26 PM, n=1	550.0 (± 99999)			
Day 27 AM, n=1	530.0 (± 99999)			
Day 27 PM, n=1	580.0 (± 99999)			
Day 28 AM, n=1	530.0 (± 99999)			
Day 28 PM, n=1	500.0 (± 99999)			

Notes:

[68] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 500 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FP 500 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 15 PM, Days 16,17,18,19,20,21 AM and PM in period 2

End point values	FP 500 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[69]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15 PM, n=6	486.7 (± 43.8)			
Day 16 AM, n=6	476.7 (± 43.8)			
Day 16 PM, n=6	503.3 (± 46.8)			
Day 17 AM, n=6	493.3 (± 44.0)			
Day 17 PM, n=6	500.0 (± 45.9)			
Day 18 AM, n=6	476.7 (± 39.9)			
Day 18 PM, n=6	495.0 (± 42.8)			
Day 19 AM, n=5	454.0 (± 44.3)			
Day 19 PM, n=6	500.0 (± 45.1)			
Day 20 AM, n=5	524.0 (± 43.6)			
Day 20 PM, n=6	501.7 (± 50.6)			
Day 21 AM, n=6	490.0 (± 44.2)			
Day 21 PM, n=6	496.7 (± 48.4)			

Notes:

[69] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 1000 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FP 1000 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed. 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:
Day 22 PM, Days 23,24,25,26,27,28,29,30,31,32,33,34,35 AM and PM in period 1

End point values	FP 1000 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	11[70]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM, n=6	523.2 (± 30.5)			
Day 23 AM, n=11	511.8 (± 36.4)			
Day 23 PM, n=11	516.4 (± 38.4)			
Day 24 AM, n=11	521.8 (± 38.0)			
Day 24 PM, n=11	520.9 (± 37.1)			
Day 25 AM, n=11	489.5 (± 35.1)			
Day 25 PM, n=10	521.0 (± 42.7)			
Day 26 AM, n=11	502.7 (± 37.0)			
Day 26 PM, n=11	517.3 (± 35.7)			
Day 27 AM, n=11	493.6 (± 33.0)			
Day 27 PM, n=11	523.6 (± 37.7)			
Day 28 AM, n=11	500.0 (± 40.6)			
Day 28,PM, n=11	516.4 (± 33.9)			
Day 29 PM, n=1	530.0 (± 99999)			
Day 30 AM, n=1	520.0 (± 99999)			
Day 30 PM, n=1	530.0 (± 99999)			
Day 31 AM, n=1	510.0 (± 99999)			
Day 31 PM, n=1	530.0 (± 99999)			
Day 32 AM, n=1	520.0 (± 99999)			
Day 32 PM, n=1	550.0 (± 99999)			
Day 33 AM, n=1	530.0 (± 99999)			
Day 33 PM, n=1	540.0 (± 99999)			
Day 34 AM, n=1	510.0 (± 99999)			
Day 34 PM, n=1	520.0 (± 99999)			
Day 35 AM, n=1	540.0 (± 99999)			
Day 35 PM, n=1	550.0 (± 99999)			

Notes:
[70] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 1000 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FP 1000 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 22 PM, Days 23,24,25,26,27,28 AM and PM in period 2

End point values	FP 1000 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[71]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM, n=6	493.3 (± 42.8)			
Day 23 AM, n=6	480.0 (± 43.4)			
Day 23 PM, n=6	506.7 (± 43.5)			
Day 24 AM, n=6	481.7 (± 39.4)			
Day 24 PM, n=6	505.0 (± 45.3)			
Day 25 AM, n=6	491.7 (± 43.9)			
Day 25 PM, n=6	510.0 (± 51.7)			
Day 26 AM, n=6	485.0 (± 45.3)			
Day 26 PM, n=6	501.7 (± 49.9)			
Day 27 AM, n=6	475.0 (± 42.3)			
Day 27 PM, n=6	490.0 (± 43.2)			
Day 28 AM, n=5	452.0 (± 47.7)			
Day 28,PM, n=5	476.0 (± 56.8)			

Notes:

[71] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 2000 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for FP 2000 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 29 PM, Days 30,31,32,33,34,35 AM and PM in period 1

End point values	FP 2000 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	10[72]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM, n=10	520.5 (± 36.5)			
Day 30 AM, n=10	505.0 (± 39.0)			
Day 30 PM, n=10	520.0 (± 40.9)			
Day 31 AM, n=10	507.0 (± 37.0)			
Day 31 PM, n=10	521.0 (± 41.7)			
Day 32 AM, n=10	500.0 (± 39.6)			
Day 32 PM, n=10	524.0 (± 41.9)			
Day 33 AM, n=10	511.0 (± 40.7)			
Day 33 PM, n=10	511.5 (± 43.2)			
Day 34 AM, n=10	519.0 (± 38.9)			
Day 34 PM, n=10	517.0 (± 38.9)			
Day 35 AM, n=9	514.4 (± 40.4)			
Day 35 PM, n=9	543.9 (± 44.1)			

Notes:

[72] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for FP 2000 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for FP 2000 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 29 PM, Days 30,31,32,33,34,35 AM and PM in period 2

End point values	FP 2000 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	6[73]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM	506.7 (± 45.8)			
Day 30 AM	493.3 (± 45.0)			
Day 30 PM	496.7 (± 46.8)			
Day 31 AM	486.7 (± 48.0)			

Day 31 PM	485.0 (± 41.6)			
Day 32 AM	488.3 (± 44.7)			
Day 32 PM	513.3 (± 52.6)			
Day 33 AM	495.0 (± 45.3)			
Day 33 PM	498.3 (± 44.1)			
Day 34 AM	481.7 (± 46.0)			
Day 34 PM	498.3 (± 47.7)			
Day 35 AM	483.3 (± 44.2)			
Day 35 PM	493.3 (± 46.3)			

Notes:

[73] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 100 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for BUD 100 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed. 99999 indicates standard error could not be calculated as only one participant was analyzed.

End point type	Secondary

End point timeframe:

Days 2 to 6 AM and PM, Day 7 PM in period 1

End point values	BUD 100 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	12[74]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2 AM, n=1	600.0 (± 99999)			
Day 2 PM, n=12	512.9 (± 33.4)			
Day 3 AM, n=1	600.0 (± 99999)			
Day 3 PM, n=12	517.1 (± 31.2)			
Day 4 AM, n=1	625.0 (± 99999)			
Day 4 PM, n=12	524.2 (± 32.9)			
Day 5 AM, n=1	600.0 (± 99999)			
Day 5 PM, n=12	520.8 (± 32.3)			
Day 6 AM, n=1	600.0 (± 99999)			
Day 6 PM, n=12	523.3 (± 33.5)			
Day 7 PM, n=12	527.5 (± 33.4)			

Notes:
[74] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 100 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for BUD 100 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 2,3,4,5,6,7 PM in period 2

End point values	BUD 100 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	4[75]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 2 PM, n=4	557.5 (± 28.3)			
Day 3 PM, n=4	547.5 (± 60.1)			
Day 4 PM, n=4	545.0 (± 27.2)			
Day 5 PM, n=4	552.5 (± 46.0)			
Day 6 PM, n=4	577.5 (± 26.5)			
Day 7 PM, n=3	603.3 (± 32.8)			

Notes:
[75] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 400 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for BUD 400 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Days 8 PM, Day 9 to 14 AM and PM in period 1

End point values	BUD 400 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	12[76]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8 PM, n=12	521.7 (± 31.5)			
Day 9 AM, n=10	473.0 (± 30.5)			
Day 9 PM, n=12	515.4 (± 34.3)			
Day 10 AM, n=10	470.0 (± 33.9)			
Day 10 PM, n=12	512.9 (± 32.8)			
Day 11 AM, n=10	466.7 (± 36.0)			
Day 11 PM, n=11	492.5 (± 35.2)			
Day 12 AM, n=9	451.1 (± 28.6)			
Day 12 PM, n=11	509.5 (± 33.7)			
Day 13 AM, n=9	457.8 (± 33.9)			
Day 13 PM, n=11	506.8 (± 33.1)			
Day 14 AM, n=11	480.5 (± 30.3)			
Day 14 PM, n=11	496.4 (± 32.1)			

Notes:

[76] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 400 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for BUD 400 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 8 PM, Days 9 to 14 AM and PM in period 2

End point values	BUD 400 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	5[77]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 8 PM	560.0 (± 43.3)			
Day 9 AM	552.0 (± 40.1)			
Day 9 PM	560.0 (± 34.7)			
Day 10 AM	552.0 (± 34.9)			

Day 10 PM	556.0 (± 30.7)			
Day 11 AM	562.0 (± 26.7)			
Day 11 PM	574.0 (± 30.4)			
Day 12 AM	568.0 (± 29.3)			
Day 12 PM	578.0 (± 44.2)			
Day 13 AM	562.0 (± 28.1)			
Day 13 PM	588.0 (± 37.6)			
Day 14 AM	586.0 (± 22.2)			
Day 14 PM	590.0 (± 44.6)			

Notes:

[77] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 800 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for BUD 800 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Days 15,16, 17, 18, 19, 20, 21 AM and PM in period 1

End point values	BUD 800 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	11[78]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15 AM, n=1	610.0 (± 99999)			
Day 15 PM, n=11	515.5 (± 30.1)			
Day 16 AM, n=11	494.5 (± 31.9)			
Day 16 PM, n=11	507.3 (± 34.9)			
Day 17 AM, n=11	484.1 (± 33.4)			
Day 17 PM, n=11	505.0 (± 34.8)			
Day 18 AM, n=11	492.7 (± 33.4)			
Day 18 PM, n=11	503.2 (± 36.4)			
Day 19 AM, n=11	483.2 (± 29.7)			
Day 19 PM, n=11	487.7 (± 38.0)			
Day 20 AM, n=11	483.6 (± 31.7)			
Day 20 PM, n=11	517.7 (± 33.9)			
Day 21 AM, n=11	490.5 (± 27.2)			
Day 21 PM, n=11	509.1 (± 32.9)			

Notes:
[78] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 800 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for BUD 800 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 15 PM, Day 16, 17, 18, 19, 20, 21 AM and PM in period 2

End point values	BUD 800 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	5[79]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 15 PM	578.0 (± 32.0)			
Day 16 AM	568.0 (± 37.6)			
Day 16 PM	572.0 (± 45.3)			
Day 17 AM	572.0 (± 27.8)			
Day 17 PM	558.0 (± 46.0)			
Day 18 AM	558.0 (± 45.8)			
Day 18 PM	568.0 (± 53.1)			
Day 19 AM	572.0 (± 46.4)			
Day 19 PM	584.0 (± 47.3)			
Day 20 AM	590.0 (± 37.6)			
Day 20 PM	590.0 (± 37.6)			
Day 21 AM	574.0 (± 23.5)			
Day 21 PM	606.0 (± 38.0)			

Notes:
[79] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 1600 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for BUD 1600 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 22 PM, Day 23,24,25,26,27,28 AM and PM in period 1

End point values	BUD 1600 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	11[80]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM	506.4 (± 33.9)			
Day 23 AM	496.4 (± 29.8)			
Day 23 PM	512.7 (± 32.3)			
Day 24 AM	498.2 (± 34.8)			
Day 24 PM	510.5 (± 34.9)			
Day 25 AM	500.5 (± 32.8)			
Day 25 PM	514.1 (± 33.2)			
Day 26 AM	499.1 (± 31.3)			
Day 26 PM	512.3 (± 35.2)			
Day 27 AM	491.4 (± 31.0)			
Day 27 PM	497.7 (± 37.3)			
Day 28 AM	476.8 (± 27.9)			
Day 28 PM	526.8 (± 33.9)			

Notes:

[80] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 1600 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for BUD 1600 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 22 PM, Days 23,24,25,26,27,28 AM and PM in period 2

End point values	BUD 1600 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	5[81]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 22 PM, n=5	594.0 (± 47.8)			
Day 23 AM, n=5	578.0 (± 40.0)			
Day 23 PM, n=5	586.0 (± 46.4)			
Day 24 AM, n=5	556.0 (± 37.8)			
Day 24 PM, n=5	556.0 (± 45.2)			
Day 25 AM, n=5	564.0 (± 50.6)			
Day 25 PM, n=5	594.0 (± 45.4)			
Day 26 AM, n=5	584.0 (± 45.6)			
Day 26 PM, n=5	568.0 (± 51.1)			
Day 27 AM, n=5	568.0 (± 52.1)			
Day 27 PM, n=5	584.0 (± 35.3)			
Day 28 AM, n=5	574.0 (± 30.1)			
Day 28 PM, n=4	630.0 (± 46.0)			

Notes:

[81] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 3200 mcg in period 1

End point title	PEFR as a measure of safety and tolerability for BUD 3200 mcg in period 1

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Day 29 PM, Day 30, 31,32,33,34,35 AM and PM in period 1

End point values	BUD 3200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	10[82]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM, n=10	493.0 (± 31.9)			
Day 30 AM, n=10	482.0 (± 33.5)			
Day 30 PM, n=10	502.0 (± 33.3)			
Day 31 AM, n=10	482.0 (± 34.0)			
Day 31 PM, n=10	496.0 (± 32.4)			
Day 32 AM, n=10	482.0 (± 30.1)			
Day 32 PM, n=10	488.0 (± 33.0)			

Day 33 AM, n=10	483.0 (± 29.1)			
Day 33 PM, n=10	490.0 (± 35.0)			
Day 34 AM, n=10	489.0 (± 31.3)			
Day 34 PM, n=9	522.2 (± 33.4)			
Day 35 AM, n=10	474.0 (± 33.8)			
Day 35 PM, n=10	488.0 (± 30.6)			

Notes:

[82] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: PEFR as a measure of safety and tolerability for BUD 3200 mcg in period 2

End point title	PEFR as a measure of safety and tolerability for BUD 3200 mcg in period 2

End point description:

PEFR is a participant's maximum speed of expiration and was measured using a peak flow meter. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed (represented by n=X in the category titles).

End point type	Secondary

End point timeframe:

Day 29 PM, Day 30, 31,32,33,34,35 AM and PM in period 2

End point values	BUD 3200 mcg			
Subject group type	Subject analysis set			
Number of subjects analysed	5[83]			
Units: Liters per minute				
arithmetic mean (standard error)				
Day 29 PM, n=5	596.0 (± 43.8)			
Day 30 AM, n=5	604.0 (± 22.7)			
Day 30 PM, n=5	586.0 (± 41.5)			
Day 31 AM, n=4	562.5 (± 33.5)			
Day 31 PM, n=4	547.5 (± 43.8)			
Day 32 AM, n=4	592.5 (± 38.6)			
Day 32 PM, n=4	587.5 (± 18.8)			
Day 33 AM, n=4	567.5 (± 30.3)			
Day 33 PM, n=4	565.0 (± 42.9)			
Day 34 AM, n=4	585.0 (± 38.4)			
Day 34 PM, n=4	583.8 (± 29.6)			
Day 35 AM, n=4	577.5 (± 35.6)			
Day 35 PM, n=4	597.5 (± 38.6)			

Notes:

[83] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal vital signs: Systolic blood pressure (SBP) and Diastolic blood pressure (DBP)

End point title	Number of participants with clinically significant abnormal vital signs: Systolic blood pressure (SBP) and Diastolic blood pressure (DBP)

End point description:

SBP and DBP were measured after participants had rested in supine position for at least 5 minutes. Results are presented treatment wise. No data collected separately for this outcome measure as any abnormal value would be recorded as an Adverse Event.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FP 200 mcg	FP 2000 mcg	BUD 100 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[84]	0[85]	0[86]	0[87]
Units: Participants				

Notes:

[84] - All Subjects Population.

[85] - All Subjects Population.

[86] - All Subjects Population.

[87] - All Subjects Population.

End point values	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg	FF 800 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[88]	0[89]	0[90]	0[91]
Units: Participants				

Notes:

[88] - All Subjects Population.

[89] - All Subjects Population.

[90] - All Subjects Population.

[91] - All Subjects Population.

End point values	Placebo	FF 25 mcg	FF 200 mcg	FP 50 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[92]	0[93]	0[94]	0[95]
Units: Participants				

Notes:

[92] - All Subjects Population.

[93] - All Subjects Population.

[94] - All Subjects Population.

[95] - All Subjects Population.

End point values	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg	FF 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[96]	0[97]	0[98]	0[99]
Units: Participants				

Notes:

[96] - All Subjects Population.

[97] - All Subjects Population.

[98] - All Subjects Population.

[99] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal vital signs: Pulse rate

End point title	Number of participants with clinically significant abnormal vital signs: Pulse rate

End point description:

Pulse rate was measured after participants had rested in supine position for at least 5 minutes. Results are presented treatment wise. No data collected separately for this outcome measure as any abnormal value would be recorded as an Adverse Event.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FP 200 mcg	FP 2000 mcg	BUD 100 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[100]	0[101]	0[102]	0[103]
Units: Participants				

Notes:

[100] - All Subjects Population.

[101] - All Subjects Population.

[102] - All Subjects Population.

[103] - All Subjects Population.

End point values	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg	FF 800 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[104]	0[105]	0[106]	0[107]
Units: Participants				

Notes:

[104] - All Subjects Population.

[105] - All Subjects Population.

[106] - All Subjects Population.

[107] - All Subjects Population.

End point values	Placebo	FF 25 mcg	FF 200 mcg	FP 50 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[108]	0[109]	0[110]	0[111]
Units: Participants				

Notes:

[108] - All Subjects Population.

[109] - All Subjects Population.

[110] - All Subjects Population.

[111] - All Subjects Population.

End point values	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg	FF 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[112]	0[113]	0[114]	0[115]
Units: Participants				

Notes:

[112] - All Subjects Population.

[113] - All Subjects Population.

[114] - All Subjects Population.

[115] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal vital signs: Respiratory rate

End point title	Number of participants with clinically significant abnormal vital signs: Respiratory rate

End point description:

Respiratory rate was measured after participants had rested in supine position for at least 5 minutes. Results are presented treatment wise. No data collected separately for this outcome measure as any abnormal value would be recorded as an Adverse Event.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FP 200 mcg	FP 2000 mcg	BUD 100 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[116]	0[117]	0[118]	0[119]
Units: Participants				

Notes:

[116] - All Subjects Population.

[117] - All Subjects Population.

[118] - All Subjects Population.

[119] - All Subjects Population.

End point values	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg	FF 800 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[120]	0[121]	0[122]	0[123]
Units: Participants				

Notes:

[120] - All Subjects Population.

[121] - All Subjects Population.

[122] - All Subjects Population.

[123] - All Subjects Population.

End point values	Placebo	FF 25 mcg	FF 200 mcg	FP 50 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[124]	0[125]	0[126]	0[127]
Units: Participants				

Notes:

[124] - All Subjects Population.

[125] - All Subjects Population.

[126] - All Subjects Population.

[127] - All Subjects Population.

End point values	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg	FF 400 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[128]	0[129]	0[130]	0[131]
Units: Participants				

Notes:

[128] - All Subjects Population.

[129] - All Subjects Population.

[130] - All Subjects Population.

[131] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with clinically significant abnormal vital signs: Temperature

End point title	Number of Participants with clinically significant abnormal vital signs: Temperature

End point description:

Temperature was measured after participants have been rested in supine position for at least 5 minutes. Results are presented treatment wise. No data collected separately for this outcome measure as any abnormal value would be recorded as an Adverse Event.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FF 400 mcg	FP 200 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[132]	0[133]	0[134]	0[135]
Units: Participants				

Notes:

[132] - All Subjects Population.

[133] - All Subjects Population.

[134] - All Subjects Population.

[135] - All Subjects Population.

End point values	BUD 100 mcg	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[136]	0[137]	0[138]	0[139]
Units: Participants				

Notes:

[136] - All Subjects Population.

[137] - All Subjects Population.

[138] - All Subjects Population.

[139] - All Subjects Population.

End point values	FF 800 mcg	Placebo	FF 25 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[140]	0[141]	0[142]	0[143]
Units: Participants				

Notes:

[140] - All Subjects Population.

[141] - All Subjects Population.

[142] - All Subjects Population.

[143] - All Subjects Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[144]	0[145]	0[146]	0[147]
Units: Participants				

Notes:

[144] - All Subjects Population.

[145] - All Subjects Population.

[146] - All Subjects Population.

[147] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with abnormal physical examination

End point title	Number of participants with abnormal physical examination

End point description:

Physical examinations included assessment of the cardiovascular, respiratory, gastrointestinal, skin, abdomen (liver and spleen), and neurological systems. This analysis was planned and data was not collected and captured in the database. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	Placebo	FF 25 mcg	FF 100 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[148]	0[149]	0[150]	0[151]
Units: Participants				

Notes:

[148] - All Subjects Population.

[149] - All Subjects Population.

[150] - All Subjects Population.

[151] - All Subjects Population.

End point values	FF 400 mcg	FF 800 mcg	FP 50 mcg	FP 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[152]	0[153]	0[154]	0[155]
Units: Participants				

Notes:

[152] - All Subjects Population.

[153] - All Subjects Population.

[154] - All Subjects Population.

[155] - All Subjects Population.

End point values	FP 500 mcg	FP 1000 mcg	FP 2000 mcg	BUD 100 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[156]	0[157]	0[158]	0[159]
Units: Participants				

Notes:

[156] - All Subjects Population.

[157] - All Subjects Population.

[158] - All Subjects Population.

[159] - All Subjects Population.

End point values	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[160]	0[161]	0[162]	0[163]
Units: Participants				

Notes:

[160] - All Subjects Population.

[161] - All Subjects Population.

[162] - All Subjects Population.

[163] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal hematology parameters

End point title	Number of participants with clinically significant abnormal hematology parameters

End point description:

Blood samples were collected for assessement of following hematology parameters: basophils, eosinophils, Erythrocyte mean corpuscular volume (MCV), hemoglobin, hematocrit, Erythrocyte mean corpuscular hemoglobin (MCH), leukocytes, lymphocytes, monocytes, platelets. Results are presented

treatment wise. Only participants with clinically significant abnormal hematology data was reported.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FF 400 mcg	FP 200 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[164]	18[165]	20[166]	17[167]
Units: Participants	0	0	0	0

Notes:

[164] - All Subjects Population.

[165] - All Subjects Population.

[166] - All Subjects Population.

[167] - All Subjects Population.

End point values	BUD 100 mcg	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[168]	18[169]	18[170]	18[171]
Units: Participants	0	0	0	0

Notes:

[168] - All Subjects Population.

[169] - All Subjects Population.

[170] - All Subjects Population.

[171] - All Subjects Population.

End point values	FF 800 mcg	Placebo	FF 25 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[172]	17[173]	20[174]	19[175]
Units: Participants	0	0	0	0

Notes:

[172] - All Subjects Population.

[173] - All Subjects Population.

[174] - All Subjects Population.

[175] - All Subjects Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21[176]	20[177]	18[178]	18[179]
Units: Participants	0	0	0	0

Notes:

[176] - All Subjects Population.

[177] - All Subjects Population.

[178] - All Subjects Population.

[179] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal chemistry parameters

End point title	Number of participants with clinically significant abnormal chemistry parameters

End point description:

Blood samples were collecte for assessment of following chemistry parametres:Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), albumin, alkaline phosphatase, bilirubin, calcium, creatinine, glucose, direct bilirubin, potassium, protein, sodium, urea. Results are presented treatment wise. Only participants with clinically significant abnormal chemistry data was reported.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FF 400 mcg	FP 200 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[180]	18[181]	20[182]	17[183]
Units: Participants	0	0	0	0

Notes:

[180] - All Subjects Population.

[181] - All Subjects Population.

[182] - All Subjects Population.

[183] - All Subjects Population.

End point values	BUD 100 mcg	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[184]	18[185]	18[186]	18[187]
Units: Participants	0	0	0	0

Notes:

[184] - All Subjects Population.

[185] - All Subjects Population.

[186] - All Subjects Population.

[187] - All Subjects Population.

End point values	FF 800 mcg	Placebo	FF 25 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[188]	17[189]	20[190]	19[191]
Units: Participants	0	0	0	0

Notes:

[188] - All Subjects Population.

[189] - All Subjects Population.

[190] - All Subjects Population.

[191] - All Subjects Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21[192]	20[193]	18[194]	18[195]
Units: Participants	0	0	0	0

Notes:

[192] - All Subjects Population.

[193] - All Subjects Population.

[194] - All Subjects Population.

[195] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with clinically significant abnormal urinalysis parameters

End point title	Number of participants with clinically significant abnormal urinalysis parameters

End point description:

Urine sample were collected to assess following urine parameters: potential of hydrogen (pH), glucose, protein, blood and ketones by dipstick. Results are presented treatment wise. Only participants with clinically significant abnormal urinalysis data was reported.

End point type	Secondary

End point timeframe:

Up to Week 18

End point values	FF 100 mcg	FF 400 mcg	FP 200 mcg	FP 2000 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[196]	18[197]	20[198]	17[199]
Units: Participants	0	0	0	0

Notes:

[196] - All Subjects Population.

[197] - All Subjects Population.

[198] - All Subjects Population.

[199] - All Subjects Population.

End point values	BUD 100 mcg	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[200]	18[201]	18[202]	18[203]
Units: Participants	0	0	0	0

Notes:

[200] - All Subjects Population.

[201] - All Subjects Population.

[202] - All Subjects Population.

[203] - All Subjects Population.

End point values	FF 800 mcg	Placebo	FF 25 mcg	FF 200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	18[204]	17[205]	20[206]	19[207]
Units: Participants	0	0	0	0

Notes:

[204] - All Subjects Population.

[205] - All Subjects Population.

[206] - All Subjects Population.

[207] - All Subjects Population.

End point values	FP 50 mcg	FP 500 mcg	FP 1000 mcg	BUD 3200 mcg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	21[208]	20[209]	18[210]	18[211]
Units: Participants	0	0	0	0

Notes:

[208] - All Subjects Population.

[209] - All Subjects Population.

[210] - All Subjects Population.

[211] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume in 1 Second (FEV 1) in Period 1

End point title	Forced Expiratory Volume in 1 Second (FEV 1) in Period 1

End point description:

FEV1 was measured with participants in a sitting position using a calibrated spirometer in accordance with American Thoracic Society (ATS) guidelines using European Respiratory Society (ERS) guidelines for predicted values. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose) in Period 1

End point values	Placebo	Fluticasone furoate (FF)	Fluticasone Furoate (FF)	Budesonide (BUD)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12[212]	14[213]	15[214]	12[215]
Units: Liter				
arithmetic mean (standard error)	3.18 (± 0.151)	3.02 (± 0.166)	3.50 (± 0.269)	3.29 (± 0.274)

Notes:

[212] - All Subjects Population.

[213] - All Subjects Population.

[214] - All Subjects Population.

[215] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Expiratory Volume in 1 Second (FEV 1) in Period 2

End point title	Forced Expiratory Volume in 1 Second (FEV 1) in Period 2

End point description:

FEV1 was measured with participants in a sitting position using a calibrated spirometer in accordance with American Thoracic Society (ATS) guidelines using European Respiratory Society (ERS) guidelines for predicted values. Results are presented treatment wise. Only those participants with data available at specified time point were analyzed.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose) in Period 2

End point values	Placebo	Fluticasone furoate (FF)	Fluticasone Propionate (FP)	Budesonide (BUD)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5[216]	6[217]	6[218]	6[219]
Units: Liter				
arithmetic mean (standard error)	2.67 (± 0.482)	3.44 (± 0.431)	2.68 (± 0.278)	3.46 (± 0.257)

Notes:

[216] - All Subjects Population.

[217] - All Subjects Population.

[218] - All Subjects Population.

[219] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Vital Capacity (FVC) in Period 1

End point title	Forced Vital Capacity (FVC) in Period 1

End point description:

FVC was measured with participants in a sitting position using a calibrated spirometer in accordance with ATS guidelines using ERS guidelines for predicted values. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose) in Period 1

End point values	Placebo	Fluticasone furoate (FF)	Fluticasone Furoate (FF)	Budesonide (BUD)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12[220]	14[221]	15[222]	12[223]
Units: Liter				
arithmetic mean (standard error)	4.55 (± 0.221)	4.36 (± 0.222)	5.15 (± 0.287)	4.70 (± 0.406)

Notes:

[220] - All Subjects Population.

[221] - All Subjects Population.

[222] - All Subjects Population.

[223] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Forced Vital Capacity (FVC) in Period 2

End point title	Forced Vital Capacity (FVC) in Period 2

End point description:

FVC was measured with participants in a sitting position using a calibrated spirometer in accordance with ATS guidelines using ERS guidelines for predicted values. Results are presented treatment wise.

End point type	Secondary

End point timeframe:

Day 1 (pre-dose) in Period 2

End point values	Placebo	Fluticasone furoate (FF)	Fluticasone Propionate (FP)	Budesonide (BUD)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	5[224]	6[225]	6[226]	6[227]
Units: Liter				
arithmetic mean (standard error)	4.11 (± 0.570)	4.85 (± 0.602)	4.09 (± 0.386)	4.90 (± 0.410)

Notes:

[224] - All Subjects Population.

[225] - All Subjects Population.

[226] - All Subjects Population.

[227] - All Subjects Population.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events and non-serious adverse events were collected up to 18 weeks.

Adverse event reporting additional description:

All subjects Population was used to collect the adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Participants received matching placebo ELLIPTA or DISKUS as total daily dose for 7 days.

Reporting group title	FF 25 mcg

Reporting group description:

Participants received placebo FF ELLIPTA 25 mcg 1 puff as total daily dose for 7 days.

Reporting group title	FF 100 mcg

Reporting group description:

Participants received FF ELLIPTA 100 mcg 1 puff PM as total daily dose for 7 days.

Reporting group title	FF 200 mcg

Reporting group description:

Participants received FF ELLIPTA 200 mcg 1 puff PM as total daily dose for 7 days.

Reporting group title	FF 400 mcg

Reporting group description:

Participants received FF ELLIPTA 200 mcg 2 puffs PM as total daily dose for 7 days.

Reporting group title	FF 800 mcg

Reporting group description:

Participants received FF ELLIPTA 200 mcg 4 puffs PM as total daily dose for 7 days.

Reporting group title	FP 50 mcg

Reporting group description:

Participants received FF DISKUS 50 mcg 1 puff PM as total daily dose for 7 days.

Reporting group title	FP 200 mcg

Reporting group description:

Participants received FF DISKUS 100 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Reporting group title	FP 500 mcg

Reporting group description:

Participants received FF DISKUS 250mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Reporting group title	FP 1000 mcg

Reporting group description:

Participants received FF DISKUS 500 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.

Reporting group title	FP 2000 mcg

Reporting group description:

Participants received FF DISKUS 500 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.

Reporting group title	BUD 100 mcg

Reporting group description:

Participants received BUD Turbuhaler 100 mcg 1 puff PM as total daily dose for 7 days.

Reporting group title	BUD 400 mcg

Reporting group description:	
Participants received BUD Turbuhaler 200 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Reporting group title	BUD 800 mcg
Reporting group description:	
Participants received BUD Turbuhaler 400 mcg 1 puff AM and 1 puff PM as total daily dose for 7 days.	
Reporting group title	BUD 1600 mcg
Reporting group description:	
Participants received BUD Turbuhaler 400 mcg 2 puff AM and 2 puff PM as total daily dose for 7 days.	
Reporting group title	BUD 3200 mcg
Reporting group description:	
Participants received BUD Turbuhaler 400 mcg 4 puffs AM and PM as total daily dose for 7 days.	

Serious adverse events	Placebo	FF 25 mcg	FF 100 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	FF 200 mcg	FF 400 mcg	FF 800 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	FP 50 mcg	FP 200 mcg	FP 500 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	FP 1000 mcg	FP 2000 mcg	BUD 100 mcg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	BUD 3200 mcg		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Placebo	FF 25 mcg	FF 100 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 17 (58.82%)	6 / 20 (30.00%)	8 / 19 (42.11%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 17 (11.76%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	4	0	0
Catheter site bruise			
subjects affected / exposed	2 / 17 (11.76%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Catheter site pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Catheter site related reaction			

subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Feeling jittery			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 17 (5.88%)	1 / 20 (5.00%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Genital discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Cough			

subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	2 / 17 (11.76%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Dry throat			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Sinonasal obstruction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Arthropod bite			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	4 / 17 (23.53%)	5 / 20 (25.00%)	3 / 19 (15.79%)
occurrences (all)	8	5	3
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dry mouth			

subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Keloid scar			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0

Skin discolouration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastroenteritis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 17 (0.00%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	1 / 17 (5.88%)	0 / 20 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	FF 200 mcg	FF 400 mcg	FF 800 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 19 (36.84%)	6 / 18 (33.33%)	7 / 18 (38.89%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 19 (10.53%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Catheter site bruise			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Catheter site related reaction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Feeling jittery			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Genital discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3
Wheezing			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Cough			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Dry throat			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinonasal obstruction			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Sinus pain			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Throat irritation			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 19 (5.26%)	2 / 18 (11.11%)	1 / 18 (5.56%)
occurrences (all)	1	2	1
Dizziness			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Dysgeusia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eyelid oedema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dry mouth			

subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Lip dry			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Keloid scar			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Skin discolouration			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	1 / 19 (5.26%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Rhinitis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 19 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gout			
subjects affected / exposed	0 / 19 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	FP 50 mcg	FP 200 mcg	FP 500 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 21 (47.62%)	4 / 20 (20.00%)	4 / 20 (20.00%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Catheter site bruise			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Catheter site related reaction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Feeling jittery			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	3 / 21 (14.29%)	1 / 20 (5.00%)	1 / 20 (5.00%)
occurrences (all)	3	1	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Genital discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	1	0	1
Wheezing			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	1 / 20 (5.00%)
occurrences (all)	3	0	1

Cough			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinonasal obstruction			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 21 (9.52%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
Dizziness			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Dry mouth			

subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	1 / 21 (4.76%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Constipation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Saliva altered			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Keloid scar			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Skin discolouration			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Skin irritation			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	0 / 21 (0.00%)	1 / 20 (5.00%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			

subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 21 (4.76%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 21 (0.00%)	0 / 20 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	FP 1000 mcg	FP 2000 mcg	BUD 100 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 18 (44.44%)	6 / 17 (35.29%)	6 / 18 (33.33%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Catheter site bruise			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Catheter site related reaction			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Catheter site swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Feeling jittery			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Genital discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 18 (11.11%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Wheezing			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0

Cough			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Asthma			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinonasal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 18 (5.56%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Arthropod bite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			

subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 18 (0.00%)	2 / 17 (11.76%)	2 / 18 (11.11%)
occurrences (all)	0	2	2
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dry mouth			

subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Keloid scar			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Skin discolouration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 18 (5.56%)	2 / 17 (11.76%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	1 / 17 (5.88%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 18 (0.00%)	0 / 17 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BUD 400 mcg	BUD 800 mcg	BUD 1600 mcg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 18 (44.44%)	5 / 18 (27.78%)	6 / 18 (33.33%)
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Catheter site bruise			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2

Catheter site related reaction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Feeling jittery			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site bruise			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Genital discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Cough			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Asthma			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dry throat			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinonasal obstruction			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Scratch			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 18 (11.11%)	3 / 18 (16.67%)	3 / 18 (16.67%)
occurrences (all)	2	3	3
Dizziness			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Eyelid oedema			
subjects affected / exposed	0 / 18 (0.00%)	1 / 18 (5.56%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	0 / 18 (0.00%)	2 / 18 (11.11%)	1 / 18 (5.56%)
occurrences (all)	0	2	1
Dry mouth			

subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Lip dry			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Saliva altered			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Keloid scar			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Skin discolouration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin irritation			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			

subjects affected / exposed	1 / 18 (5.56%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Urinary tract infection			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 18 (0.00%)	0 / 18 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	BUD 3200 mcg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 18 (16.67%)		
Vascular disorders			
Phlebitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Surgical and medical procedures			
Tooth repair			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Catheter site bruise			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Catheter site pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

Catheter site related reaction subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Catheter site swelling subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Fatigue subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Feeling jittery subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Vessel puncture site bruise subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Genital discomfort subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Wheezing subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		

Cough subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Asthma subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Nasal congestion subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Dry throat subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Sinonasal obstruction subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Sinus pain subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Throat irritation subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Arthropod bite subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Scratch			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Paraesthesia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Eyelid oedema			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Dry mouth			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Lip dry			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Saliva altered			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Keloid scar			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

Skin discolouration			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin irritation			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Arthralgia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal discomfort			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastroenteritis			

subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Gout subjects affected / exposed occurrences (all)	 0 / 18 (0.00%) 0 0 / 18 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2017	Amendment No. 1 was to clarify the doserationale, emergency unblinding procedure, and approval of substantial amendments procedure, as requested by the Medicines and Healthcare products Regulatory Agency(MHRA), as well as to clarify the blood sample time points and volumes and update the medical monitor contact details.
03 October 2017	Amendment No. 2 The protocol design, to allow participants to complete either 1 or 2 treatment periods.To allow recruitment of participants taking low dose inhaled corticosteroids (ICS) with appropriate washout period. To allow inclusion of light smokers.Removal of the Run-in and treatment period 2 baseline visits for AMP challenge. To allow the subjects to leave the unit after Day 7 evening procedures. To allow in-stream data review.Changes laid down in memorandum (MEMOs) to protocol amendment 1 were also incorporated into this protocol amendment.
26 April 2018	Amendment No. 3 is being issued to update the SAE contact and processing information, the pregnancy reporting timelines, as well as to include administrative changes clarifying the screening PEFR procedure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported