



Clinical trial results:

Application of Chronotherapy to Asthma: Towards the Personalisation of Asthma Management.

A randomised, mechanistic study of 400mcg Clenil® Modulite® (Beclometasone dipropionate) in the morning versus in the afternoon versus 200mcg twice a day, in Subjects with Atopic Mild to Moderate Asthma

Summary

EudraCT number	2019-004309-28
Trial protocol	GB
Global end of trial date	22 September 2022

Results information

Result version number	v1 (current)
This version publication date	05 April 2024
First version publication date	05 April 2024
Summary attachment (see zip file)	Draft manuscript (Chronotherapy manuscript_Endura.docx)

Trial information

Trial identification

Sponsor protocol code	MEU19/383
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	MEU: MEU 19/383

Notes:

Sponsors

Sponsor organisation name	Medicines Evaluation Unit
Sponsor organisation address	Southmoor Road, Wythenshawe, United Kingdom, M239QZ
Public contact	Nicole Yan , The Medicines Evaluation Unit (MEU) Ltd. (Investigator led study), 0161 9464055, nyan@meu.org.uk
Scientific contact	Nicole Yan , The Medicines Evaluation Unit (MEU) Ltd. (Investigator led study), 0161 9464055, nyan@meu.org.uk

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	Interim
Date of interim/final analysis	21 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 September 2022
Global end of trial reached?	Yes
Global end of trial date	22 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether in asthma it is more efficacious to take inhaled corticosteroid in the morning, in the afternoon or in divided doses both in the morning and afternoon.

Efficacy will be assessed through the measurement of airway narrowing and airway inflammation

Protection of trial subjects:

Treated in routine care

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2020
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: 25
Worldwide total number of subjects	25
EEA total number of subjects	0

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)	25
From 65 to 84 years	0

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

Of 25 participants consented into the study, 22 completed morning dosing, 21 afternoon dosing and 23 twice daily dosing. Overall 21 subjects were compared across all 3 treatment groups for our analysis.

Pre-assignment

Screening details:

27 subjects were screened and 25 were included in the final study.

Pre-assignment period milestones

Number of subjects started	25
Number of subjects completed	25

Period 1

Period 1 title	Baseline (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	No
Arm title	Morning or afternoon or twice daily dosing with BDP 400mcg BDP

Arm description:

Participant was randomised to receive 400mcg BDP either in the morning or in the afternoon or twice a day, followed by a wash out period of 2 weeks and then randomised to the second treatment, washed out and then received the third treatment.

Arm type	Active comparator
Investigational medicinal product name	Becloethasone BDP
Investigational medicinal product code	
Other name	Clenil
Pharmaceutical forms	Inhalation vapour
Routes of administration	Inhalation use

Dosage and administration details:

400mcg taken at 0800-0900 morning dosing

Arm title	Baseline
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Arm description:

Baseline-after washout

Arm type	No intervention
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No investigational medicinal product assigned in this arm

Number of subjects in period 1	Morning or afternoon or twice daily dosing with BDP 400mcg BDP	Baseline
Started	25	25
Nil	21	25
Completed	21	25
Not completed	4	0
COVID	3	-
family bereavement	1	-

Baseline characteristics

Reporting groups

Reporting group title	Baseline
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Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	25	25	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	25	25	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	42		
inter-quartile range (Q1-Q3)	34 to 52	-	
Gender categorical			
Units: Subjects			
Female	9	9	
Male	16	16	

End points

End points reporting groups

Reporting group title	Morning or afternoon or twice daily dosing with BDP 400mcg BDP
Reporting group description: Participant was randomised to receive 400mcg BDP either in the morning or in the afternoon or twice a day, followed by a wash out period of 2 weeks and then randomised to the second treatment, washed out and then received the third treatment.	
Reporting group title	Baseline
Reporting group description: Baseline-after washout	

Primary: Spirometry

End point title	Spirometry
End point description: Pre-specified primary end points included the treatment differences for FEV1, PEF and FeNO changes from baseline. The key secondary end points were the treatment differences in the changes in blood eosinophil counts, serum cortisol levels and ACQ-6, reliever medication use and AE. The daily rhythms in lung function parameters, FeNO, blood eosinophil counts and serum cortisol levels were examined.	
End point type	Primary
End point timeframe: Baseline compared to end of each treatment period	

End point values	Morning or afternoon or twice daily dosing with BDP 400mcg BDP	Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	25		
Units: litres				
number (not applicable)	21	25		

Statistical analyses

Statistical analysis title	FEV1
Comparison groups	Morning or afternoon or twice daily dosing with BDP 400mcg BDP v Baseline
Number of subjects included in analysis	46
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Mean difference (final values)

Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard error of the mean

Secondary: Blood Eosinophils

End point title	Blood Eosinophils
End point description:	
End point type	Secondary
End point timeframe:	
Compare each treatment period to baseline	

End point values	Morning or afternoon or twice daily dosing with BDP 400mcg BDP	Baseline		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	25		
Units: cells/ml				
number (not applicable)	21	25		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Within study end point

Assessment type	Systematic
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Dictionary used

Dictionary name	Diamond Pharma
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Dictionary version	1
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Reporting groups

Reporting group title	Afternoon dosing
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Reporting group description: -

Serious adverse events	Afternoon dosing		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 25 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Afternoon dosing		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)		
Skin and subcutaneous tissue disorders			
Dry mouth	Additional description: 55 possible AEs were reported, only 1 was thought related to the IMP-dry mouth.		
subjects affected / exposed	1 / 25 (4.00%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
01 May 2020	COVID 19	01 February 2021

Notes:

Limitations and caveats

None reported