Clinical trial results:
CONNected Electronic Inhalers Asthma Control Trial 3 (“CONNECT 3”), a 24-Week Treatment, Multicenter, Open-Label, Randomized, Parallel Group Comparison Study of Standard of Care Treatment Versus the Budesonide/Formoterol Digihaler Digital System, to Optimize Outcomes in Adult Patients with Asthma

Summary

EudraCT number	2021-003951-41
Trial protocol	NL
Global end of trial date	29 June 2023

Results information

Result version number	v1 (current)
This version publication date	08 June 2024
First version publication date	08 June 2024

Trial information

Trial identification

Sponsor protocol code	BFS-AS-40184

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Teva Branded Pharmaceutical Products R&D, Inc.
Sponsor organisation address	145 Brandywine Parkway, West Chester, United States, 19380
Public contact	Director, Clinical Research, Teva Branded Pharmaceutical Products R&D, Inc., MedInfo@tevaeu.com
Scientific contact	Director, Clinical Research, Teva Branded Pharmaceutical Products R&D, Inc., MedInfo@tevaeu.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	01 August 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 June 2023
Global end of trial reached?	Yes
Global end of trial date	29 June 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to demonstrate the effectiveness of the Budesonide/Formoterol (BF) Digihaler Digital System (DS) compared to the Standard of Care (SoC) treatment group.

Protection of trial subjects:

This clinical study was conducted in accordance with current Good Clinical Practice (GCP) as directed by the provisions of the International Council for Harmonisation (ICH); United States (US) Code of Federal Regulations (CFR), and European Union (EU) Directives and Regulations (as applicable in the region of the study); national country legislation; and the sponsor's Standard Operating Procedures (SOPs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 January 2023
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: 5
Worldwide total number of subjects	5
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)	3
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled and randomized in 2 groups: BF Digihaler DS group and SoC group. A total of 5 participants were randomized; 3 in the SoC group and 2 in the BF Digihaler DS group. One participant from BF Digihaler DS group was excluded from the intent-to-treat (ITT) analysis set due to protected health information (PHI) exposure.

Pre-assignment

Screening details:

Due to trial cancellation, no participants reached the end of the 24-week treatment period, and no efficacy data were collected or evaluated.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Standard of Care (SoC)

Arm description:

Participants were treated with their current SoC treatment (prescribed by the investigational center to the participant based on asthma guidelines and clinician judgement) and did not use the digital system during the treatment period. SoC treatment included current rescue medication, inhaled corticosteroid (ICS)/ long acting beta2 agonist (LABA) and any additional controller medication for asthma.

Arm type	Active comparator
Investigational medicinal product name	ICS/LABA combinations
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation solution
Routes of administration	Inhalation use

Dosage and administration details:

Participants were treated with their current SoC treatment (prescribed by the investigational center to the participant based on asthma guidelines and clinician judgement).

Arm title	Digital System (DS)

Arm description:

Participants were trained on the use of the BF Digihaler (including instructions on how to use the inhaler and the App). Upon demonstrating competency, participants had their maintenance ICS with LABA, and rescue medication or ICS/formoterol maintenance and reliever therapy (MART) switched to the BF Digihaler given as MART (at a dose of BF comparable to their most recent current ICS dose). The BF Digihaler DS consisted of 4 devices: Device 1: BF Digihaler used as MART; Device 2: Patient-facing mobile phone App; Device 3: Digital Health Platform (DHP) (Cloud solution); and Device 4: Healthcare Professional (HCP)-facing dashboard. Participants received budesonide/formoterol 1 to 2 oral inhalations twice daily, based on the equivalent dose of ICS previously used.

Arm type	Experimental
Investigational medicinal product name	Budesonide/Formoterol Digihaler Digital System
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Inhalation powder
Routes of administration	Inhalation use

Dosage and administration details:

Participants received budesonide/formoterol 1 to 2 oral inhalations twice daily, based on the equivalent dose of ICS previously used.

Number of subjects in period 1[1]	Standard of Care (SoC)	Digital System (DS)
Started	3	1
Received at least 1 dose of study drug	3	1
Completed	0	0
Not completed	3	1
Adverse event, non-fatal	-	1
Sponsor request	3	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One participant from BF Digihaler DS group was excluded from the ITT analysis set due to PHI exposure.

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study
Reporting group description:	
All enrolled participants who were randomized to either Standard of Care (SoC) group or Digital System (DS) group.	

Reporting group values	Overall Study	Total	
Number of subjects	4	4	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	47.3		
standard deviation	± 14.20	-	
Gender Categorical Units: Subjects			
Female	1	1	
Male	3	3	
Ethnicity Units: Subjects			
Not reported	4	4	
Race Units: Subjects			
White	4	4	

End points

End points reporting groups

Reporting group title	Standard of Care (SoC)

Reporting group description:

Participants were treated with their current SoC treatment (prescribed by the investigational center to the participant based on asthma guidelines and clinician judgement) and did not use the digital system during the treatment period. SoC treatment included current rescue medication, inhaled corticosteroid (ICS)/ long acting beta2 agonist (LABA) and any additional controller medication for asthma.

Reporting group title	Digital System (DS)

Reporting group description:

Participants were trained on the use of the BF Digihaler (including instructions on how to use the inhaler and the App). Upon demonstrating competency, participants had their maintenance ICS with LABA, and rescue medication or ICS/formoterol maintenance and reliever therapy (MART) switched to the BF Digihaler given as MART (at a dose of BF comparable to their most recent current ICS dose). The BF Digihaler DS consisted of 4 devices: Device 1: BF Digihaler used as MART; Device 2: Patient-facing mobile phone App; Device 3: Digital Health Platform (DHP) (Cloud solution); and Device 4: Healthcare Professional (HCP)-facing dashboard. Participants received budesonide/formoterol 1 to 2 oral inhalations twice daily, based on the equivalent dose of ICS previously used.

Primary: Number of Participants Achieving Well-Controlled Asthma or Reaching Clinically Important Improvement in Asthma Control

End point title	Number of Participants Achieving Well-Controlled Asthma or Reaching Clinically Important Improvement in Asthma Control[1]

End point description:

Well-controlled asthma is defined by an asthma control test (ACT) score of greater than or equal to 20. Clinically important improvement in asthma control is defined by an increase of at least 3 ACT units from baseline at the end of the 24-week treatment period. The ACT is a simple, participant-completed tool used for the assessment of overall asthma control. The ACT includes 5 items that assess daytime and nighttime asthma symptoms, use of reliever medication, and impact of asthma on daily functioning. Each item in the ACT is scored on a 5-point scale ranging from 1 (poor control of asthma) to 5 (well control of asthma), with summation of all items providing scores ranging from 5 to 25. The scores span the continuum of poor control of asthma (score of 5) to complete control of asthma (score of 25), with a cutoff score of 19 and below indicating participants with poorly controlled asthma.

End point type	Primary

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to trial cancellation, no participants reached the end of the 24-week treatment period, and no efficacy data were collected or evaluated.

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[2]	0[3]		
Units: participants				

Notes:

[2] - Due to trial cancellation, no efficacy data were collected or evaluated.

[3] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Discussions Between Participant and Investigational Center Healthcare Professional (iHCP) Regarding Inhaler Technique and Regarding Adherence

End point title	Number of Discussions Between Participant and Investigational Center Healthcare Professional (iHCP) Regarding Inhaler Technique and Regarding Adherence

End point description:

Number of participants who had discussions with iHCP regarding inhaler technique and adherence was to be reported.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[4]	0[5]		
Units: participants				

Notes:

[4] - Due to trial cancellation, no efficacy data were collected or evaluated.

[5] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Different Frequency of Intervention to Manage Comorbid Conditions Associated With Poor Asthma Control

End point title	Number of Participants With Different Frequency of Intervention to Manage Comorbid Conditions Associated With Poor Asthma Control

End point description:

Number of participants with different frequency of intervention to manage comorbid conditions associated (such as gastroesophageal reflux disease, sinusitis, etc.) with poor asthma control was to be reported.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	0[7]		
Units: participants				

Notes:

[6] - Due to trial cancellation, no efficacy data were collected or evaluated.

[7] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Adjustments of Therapy

End point title	Number of Adjustments of Therapy

End point description:

Number of adjustments of therapy included: Changes to current inhaler therapy (stepping up and stepping down); Change to different inhaled medication; Additional inhaled medication; and Addition of a systemic corticosteroid medication for asthma or another controller, including LAMA or biologics.

End point type	Secondary

End point timeframe:

Baseline up to Week 24

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[8]	0[9]		
Units: participants				

Notes:

[8] - Due to trial cancellation, no efficacy data were collected or evaluated.

[9] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse events (AEs) or Adverse Device Effects Related to BF Digihaler DS

End point title	Number of Participants With Adverse events (AEs) or Adverse Device Effects Related to BF Digihaler DS

End point description:

An AE was defined as any untoward medical occurrence that develops or worsens in severity during the conduct of a clinical study and does not necessarily have a causal relationship to the study drug. Serious adverse events (SAEs) included death, a life-threatening AE, inpatient hospitalization or prolongation of existing hospitalization, persistent or significant disability or incapacity, a congenital anomaly or birth defect, or an important medical event that jeopardized the participant and required medical intervention to prevent 1 of the outcomes listed in this definition. A summary of serious and non-serious AEs regardless of causality is located in 'Reported Adverse Events module'. Number of participants with any AEs, and device-related AEs has been reported. The intent-to-treat (ITT) analysis set included all randomized participants.

End point type	Secondary

End point timeframe:

From first dose of study drug until 2 weeks after end of treatment/early termination (up to Day 152)

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	1		
Units: participants				
Any AEs	2	1		
Device-related AEs	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire Score at Week 24

End point title	Change From Baseline in the Work Productivity and Activity Impairment (WPAI) Questionnaire Score at Week 24

End point description:

The WPAI questionnaire is used to measure work productivity and activity impairment. Four metrics are included: work time missed (absenteeism), impairment while working (presenteeism or reduced on-the-job effectiveness), overall work impairment (WI) (work productivity loss or absenteeism plus presenteeism) and activity impairment (daily activity impairment). Total score and each score ranges from 0 (not affected/no impairment) to 100 (completely affected/impaired). Higher scores indicate greater impairment and less productivity.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Standard of Care (SoC)	Digital System (DS)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[10]	0[11]		
Units: units on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[10] - Due to trial cancellation, no efficacy data were collected or evaluated.

[11] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Adherence to the BF Digihaler DS When Prescribed as Maintenance Treatment at Week 24

End point title	Change From Baseline in Adherence to the BF Digihaler DS When Prescribed as Maintenance Treatment at Week 24[12]

End point description:

Adherence to maintenance treatment was defined as the percentage of actual inhalation doses taken out of the total number of inhalation doses prescribed over the 24-week treatment period.

End point type	Secondary

End point timeframe:

Baseline, Week 24

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting statistics for 'Digital System (DS)' arm only.

End point values	Digital System (DS)			
Subject group type	Reporting group			
Number of subjects analysed	0[13]			
Units: percentage of inhalation				
arithmetic mean (standard deviation)	()			

Notes:

[13] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Secondary: System Usability Scale (SUS) Score at Week 24 for the BF Digihaler DS Group

End point title	System Usability Scale (SUS) Score at Week 24 for the BF Digihaler DS Group[14]

End point description:

The SUS is used to explore device acceptability and usability for participants in the BF Digihaler DS group. It covers a variety of aspects of system usability, such as the need for support, training, and complexity, and thus giving a global view of subjective assessments of usability. It is a 10-question tool (with five response options; from 1=strongly disagree to 5=strongly agree) that provides a composite measure, ranging from 0 to 100, of the overall usability of the system being studied. Higher scores represent a better usability level for the tool.

End point type	Secondary

End point timeframe:

Week 24

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting statistics for 'Digital System (DS)' arm only.

End point values	Digital System (DS)			
Subject group type	Reporting group			
Number of subjects analysed	0[15]			
Units: units on a scale				
arithmetic mean (standard deviation)	()			

Notes:

[15] - Due to trial cancellation, no efficacy data were collected or evaluated.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until 2 weeks after end of treatment/early termination (up to Day 152)	
Adverse event reporting additional description:	
The ITT analysis set included all randomized participants.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	Digital System (DS)
Reporting group description:	
Participants were trained on the use of the BF Digihaler (including instructions on how to use the inhaler and the App). Upon demonstrating competency, participants had their maintenance ICS with LABA, and rescue medication or ICS/formoterol MART switched to the BF Digihaler given as MART (at a dose of BF comparable to their most recent current ICS dose). The BF Digihaler DS consisted of 4 devices: Device 1: BF Digihaler used as MART; Device 2: Patient-facing mobile phone App; Device 3: DHP (Cloud solution); and Device 4: HCP-facing dashboard. Participants received budesonide/formoterol 1 to 2 oral inhalations twice daily, based on the equivalent dose of ICS previously used.	
Reporting group title	Standard of Care (SoC)
Reporting group description:	
Participants were treated with their current SoC treatment (prescribed by the investigational center to the participant based on asthma guidelines and clinician judgement) and did not use the digital system during the treatment period. SoC treatment included current rescue medication, ICS/LABA and any additional controller medication for asthma.	

Serious adverse events	Digital System (DS)	Standard of Care (SoC)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)	0 / 3 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Digital System (DS)	Standard of Care (SoC)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)	2 / 3 (66.67%)	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 1 (100.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 1 (100.00%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	0 / 1 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 March 2022	The primary reason for this amendment was to clarify the secondary objective - measuring device defects relating to the Digital System (software/dashboard/app), which was required by the Medicines and Healthcare products Regulatory Agency (MHRA). The device of BF Digihaler in the secondary objective, as well as throughout the protocol where applicable, was stated precise as BF Digihaler Digital System (BF Digihaler DS). In addition, conducting the semi-structured participant experience interviews was not feasible for this study and therefore was removed from the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was terminated early due to Teva’s business considerations. The decision to terminate the study was not related to any safety issues or concerns.

Notes: