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A clinical trial, involving several sites in several countries, with a duration of 12 weeks, where patients, medical doctors and the sponsor do not know the treatment taken by the patient (between one study treatment and another one) with the scope of evaluating the safety of study treatment in comparison with another similar one in subjects with asthma.

Submission date 21/07/2023	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 29/02/2024	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 08/07/2025	**Condition category** Respiratory	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a clinical trial, involving several sites in several countries, with a duration of 12 weeks, where patients, medical doctors and the sponsor do not know the treatment taken by the patient (between one study treatment and another one) with the scope of evaluating the safety of study treatment in comparison with another similar one in subjects with asthma.

Who can participate?
Patients aged between 18 and 75 years old with asthma

What does the study involve?
Not provided at time of registration

What are the possible benefits and risks of participating?
Propellant HFA-152a: Changes in your ability to feel the taste, Coughing, Dysphonia (voice impairment), Wheezing, or shortness of breath in case of narrowing of the airways (bronchoconstriction). These potential side effects are expected to be rapidly reversible and mild. The study doctor will administer rescue medications to resolve discomfort if deemed necessary.

Study Drug:
Common: urinary tract infection, inflammation of the back of the throat, oral fungal infection, runny or stuffy nose, sneezing, sore throat, headache and voice alteration (hoarseness).
Uncommon: flulike symptoms, trembling, dizziness, inflammation of the ear, irregular heartbeat, changes in the electrocardiogram (ECG), unusual fast heartbeat, feeling your heartbeat, increase of blood flow to certain tissues in the body, high blood pressure, throat irritation, oral fungal infection, oesophageal thrush, inflammation of the paranasal sinuses, irritation and inflammation of the mucous membrane inside the nose, vaginal thrush, diarrhoea, dry mouth, difficulty swallowing, nausea, stomach discomfort after meals, burning sensation of the lips, abnormal or reduced sense of taste, numbness, cough and productive cough, nose bleeds, dental caries, mouth inflammation (stomatitis), allergic inflammation of the skin, rash, hives, itching, excessive sweating, muscle spasms, pain in arms or legs, pain in muscles, bones or joints of the chest, restlessness, tiredness, weakness, changes in blood components (decrease in white blood cells, increase in platelets, decrease of potassium, increase of sugar level, increase of insulin level, increase of fatty acids, increase of ketones, increase of C-reactive protein, decrease of cortisol level in blood).
Rare: fungal infections of the chest, hypersensitivity reactions including erythema, lips, face, eye and pharyngeal oedema, decreased appetite, sleep disorders (sleeping too little or too long), crushing chest pain, unusually slow heartbeats, leakage of blood from a vessel into the tissues surrounding it, asthma exacerbation, pain in the back of the mouth and throat, dry throat, inflammation and redness of the pharynx, inflammation of the kidneys, painful and frequent urination, difficulty and pain when passing urine, weakness, increase or decrease in blood pressure.
Very rare: Glaucoma (an eye disease causing damage to the optic nerve), cataract (a cloudy area in the lens of the eye that leads to a decrease in vision), feeling breathless or short of breath, swelling of the hands and feet, bone density decreased, low level in the number of certain blood cells called platelets, inadequate production of cortisol. Side effects with unknown frequency: psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children), and blurred vision.

Most of the described side effects were reported after chronic use of the study drug with propellant.
Rescue medication can be used.

Where is the study run from?
Chiesi Farmaceutici S.p.A. (Italy)

When is the study starting and how long is it expected to run for?
July 2023 to February 2025

Who is funding the study?
Chiesi Farmaceutici S.p.A. (Italy)

Who is the main contact?
clinicaltrials_info@chiesi.com

Contact information

Type(s)
Scientific

Contact name
Dr Selene Parenti

Contact details
CROMSOURCE S.r.l. (a ClinChoice Company)
Via G. De Sandre 3
37135
Italy
Verona
+39 3665759430
Selene.Parenti@clinchoice.com

Type(s)
Principal investigator

Contact name
Dr Dave Singh

Contact details
The Langley Building
Southmoor Road
Wythenshawe
Manchester
United Kingdom
M23 9QZ
-
DSingh@meu.org.uk

Type(s)
Public

Contact name
Dr Global Clinical Development Chiesi Farmaceutici Spa

Contact details
Via Palermo 26 A
Parma
Italy
43122
-
clinicaltrials_info@chiesi.com

Additional identifiers

Clinical Trials Information System (CTIS)
2023-503333-22

Integrated Research Application System (IRAS)
1008211

ClinicalTrials.gov (NCT)
NCT06264674

Protocol serial number
CLI-05993AB6-03, IRAS 1008211, CPMS 56827

Study information

Scientific Title
A 12-week double-blind, multicentre, randomised, active-controlled, 2-arm, parallel-group clinical trial to evaluate the safety of CHF5993 pMDI 200/6/12.5 µg HFA-152a, compared to CHF5993 pMDI 200/6/12.5 µg HFA-134a, in subjects with asthma

Acronym
TRECOS

Study objectives
To compare the potential for bronchoconstriction with CHF5993 pMDI formulated using the HFA-152a propellant versus CHF5993 pMDI formulated using the HFA-134a propellant both at the 200/6/12.5 µg/actuation dosage.

To evaluate the safety and tolerability profile of HFA-152a propellant compared to HFA-134a propellant when administered as CHF5993 pMDI 200/6/12.5 µg in adults with moderate to severe controlled asthma.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 13/11/2023, Seasonal Research Ethics Committee (Research Ethics Committee Centre 2nd Floor 2 Redman Place Stratford , London, E20 1JQ, United Kingdom; 02071048129; seasonal.rec@hra.nhs.uk), ref: 23/LO/0691
2. Approved 17/01/2024, London - City & East Research Ethics Committee (Research Ethics Committee Centre 2nd Floor 2 Redman Place Stratford , London, E20 1JQ, United Kingdom; 0207 104 8124; cityandeast.rec@hra.nhs.uk), ref: 23/LO/0691

Study design
12-week double-blind multicentre randomized active-controlled two-arm parallel-group clinical trial

Primary study design
Interventional

Study type(s)
Safety

Health condition(s) or problem(s) studied
Asthma

Interventions

This study will be composed of a 2-week run-in period with CHF5993 200/6/12.5 µg fixed combination of BDP 200 µg + FF 6 µg + GB 12.5 µg, via pMDI with HFA-134a propellant (then refer as Reference product). This will be followed by a 12-week treatment period with CHF5993 200/6/12.5 µg fixed combination of BDP 200 µg + FF 6 µg + GB 12.5 µg, via pMDI with HFA-152a propellant (then refer as Test product) and Reference. Subjects will be centrally assigned through an IRT system to one of the two treatment arms in a 2:1 ratio for the Test product or Reference product An expected total duration of study participation (including pre-screening /screening and follow-up) is 16 weeks. In both treatment arms (test and reference product) the subject will be requested to take 2 inhalations twice daily (BID; i.e., 2 inhalations in the morning and 2 inhalations in the evening), with a total daily dose of BDP/FF/GB: 800/24/50 µg (subjects who inhale pMDI medications with a spacer should continue using the spacer AeroChamber Plus). The study involves a pre-screening visit, a screening visit, and then a treatment phase with four on-site visits, for up to 12 weeks. A follow-up call will be done with subjects 7 to 10 days after a subject's last intake of the study treatment to collect information on the subjects' concomitant medications/procedures and adverse events (AEs).

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
CHF5993 pMDI-152a [beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium bromide], CHF5993 pMDI-134a [beclometasone dipropionate, formoterol fumarate dihydrate, glycopyrronium bromide]

Primary outcome(s)
Potential for bronchoconstriction of each study treatment, defined as the relative change from pre-dose in FEV1 at the 10 min post-dose timepoint on Day 1

Key secondary outcome(s))
1. Relative change from pre-dose in FEV1 at all the post-dose timepoints at each study visit on Day 1, Day 7 and Week 12: 20 min, 30 min, 1 h and 2 h post-dose Day 7, Week 4 and Week 12: 10 min post-dose
2. Absolute change from pre-dose in FEV1 at all post-dose timepoints at each study visit on Day 1, Day 7, and Week 12: 10 min, 20 min, 30 min, 1 h, and 2 h post-dose Week 4: 10 min post-dose
3. Number and percentage of subjects with a relative decrease from pre-dose in FEV1 at each post-dose timepoint and at any post-dose timepoint > 15% at each study visit on Day 1, Day 7, and Week 12: 10 min, 20 min, 30 min, 1 h, and 2 h post-dose Week 4: 10 min post-dose
4. Absolute and relative changes from baseline i.e., pre-dose* FEV1 at Day 1. in pre-dose* FEV1 at all clinical visits
5. Change from pre-dose in FEV1 area under the curve from time zero to 2 h (AUC0-2h. on Day 1, Day 7 and Week 12
6. Change from baseline at each inter-visit period and over the entire treatment period in morning and evening peak expiratory flow rate (PEF)
7. Change from baseline at each inter-visit period and over the entire treatment period in the percentage of days without the intake of rescue medication
8. Change from baseline at each inter-visit period and over the entire treatment period in the average daily use of rescue medication (number of inhalations/day)
9. Change from baseline at each inter-visit period and over the entire treatment period in the

average daily symptoms
10. Change from baseline in ACQ-7 at each study visit
11. AEs and adverse drug reactions (ADRs)
12. AEs of particular interest: cough, dysphonia, paradoxical bronchospasm, hypersensitivity reactions, severe asthma exacerbations according to ATS/ERS criteria
13. Vital signs (systolic and diastolic blood pressure)
14. 12-lead ECG parameters: heart rate (HR), QTcF, PR interval (PR) and QRS interval (QRS)
15. 12-lead ECG abnormalities
16. Standard haematology and blood chemistry (including serum potassium and plasma glucose)
17. Chemistry in urine (quantitative [proteins] and qualitative [ketones and microscopic examination of the sediments])

Completion date
24/02/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/05/2024:
1. Male and female adults aged ≥18 and ≤75 years
2. Body mass index (BMI) within the range of 18.0 to 35.0 kg/m2
3. Physician-diagnosed asthma >6 months and diagnosis before 50 years
4. Stable asthma therapy: a stable treatment with medium/high doses of ICS+LABA+LAMA (fixed or free combination) or medium/high doses of ICS+LABA (fixed or free combination) for at least 4 weeks before screening
5. Asthma control: controlled or partly controlled based on an Asthma Control Questionnaire (ACQ-7) score <1.5 at screening and at randomization;
6. Pre-bronchodilator 40% < FEV1 < 90% of their predicted normal value, after appropriate washout from bronchodilators, at the screening and randomization;
7. Subjects with a positive reversibility test at screening defined as an increase ≥ 12% and/or 200 mL within 15-20 minutes after inhalation of 400mcg salbutamol [Note 1: To assess for BD response, pre-BD and post-BD spirometry must meet the acceptability and repeatability criteria as reported in the 2019 ATS/ERS Standardisation of Spirometry Update. Note 2: In case the BD response threshold is not met at a screening or if spirometry does not meet quality requirements, the spirometry test can be repeated no later than 1 day before randomisation at a second spirometry visit. In case the BD response is not met at this second spirometry visit or if spirometry does not meet quality requirements, historical documentation of BD response can be provided. Historical documentation of BD response, defined according to the 2005 American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines or history of positive bronchial challenge test (methacholine) within 24months prior to screening, is also accepted. Copy of original printed spirometry or bronchial challenge test must be included as source documentation.]

Previous inclusion criteria:
1. Male and female adults aged ≥18 and ≤75
2. Body mass index (BMI) within the range of 18.0 to 35.0 kg/m2
3. Physician-diagnosed asthma >6 months and diagnosis before 50 years
4. Stable asthma therapy: a stable treatment with medium/high doses of ICS+LABA+LAMA (fixed or free combination) or medium/high doses of ICS+LABA (fixed or free combination) for at least 4 weeks before screening
5. Asthma control: controlled or partly controlled based on an Asthma Control Questionnaire

(ACQ-7) score <1.5 at screening and at randomization;
6. Pre-bronchodilator 40% < FEV1 < 90% of their predicted normal value, after appropriate washout from bronchodilators, at the screening and randomization;
7. Subjects with a positive reversibility test at screening defined as an increase ≥ 12% and/or 200 mL within 15-20 minutes after inhalation of 400mcg salbutamol [NOTE: in case the bronchodilator (BD) response threshold is not met at screening, the spirometry test can be repeated no later than 1 day before randomisation at a second spirometry visit. In case the BD response is not met at this second spirometry visit, historical documentation of the BD response can be provided. Historical documentation of BD response defined according to the 2005 American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force on interpretative strategies for lung function tests, or history of positive bronchial challenge test (methacholine) within 24 months prior to screening (copy of original printed spirometry to be included as source documentation) is also accepted.]

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
836

Key exclusion criteria
1. History of near-fatal asthma, hospitalisation for asthma in intensive care unit which in the judgement of the Investigator may place the subject at undue risk, emergency room access for asthma in the previous 6 months before enrolment
2. Asthma exacerbation requiring systemic corticosteroids (SCS) or emergency room admission or hospitalisation within 4 weeks prior to study entry and/or during the run-in period (to be checked again prior to randomisation)
3. Non-permanent asthma: exercise-induced, seasonal asthma (as the only asthma-related diagnosis) not requiring daily asthma control medicine
4. Asthma subjects currently treated with chronic SCS, anti-immunoglobulin E (IgE), or any other biologic therapy
5. Any concomitant respiratory disease that, in the opinion of the Investigator and/or Medical Monitor, will interfere with the evaluation of the investigational product or interpretation of subject safety or study results. This can include but is not limited to the diagnosis of chronic obstructive pulmonary disease (COPD) as defined by the current guidelines

Date of first enrolment
13/11/2023

Date of final enrolment
30/11/2024

Locations

Countries of recruitment
United Kingdom

Armenia

Bulgaria

Czech Republic

Georgia

Germany

Greece

Hungary

Italy

Netherlands

Poland

Romania

Serbia

Slovakia

Spain

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Chiesi (Italy)

ROR
https://ror.org/0511bn634

Funder(s)

Funder type
Industry

Funder Name
Chiesi Farmaceutici

Alternative Name(s)
Chiesi Pharmaceuticals, CHIESI Farmaceutici S.p.A., CHIESI, CHIESI GROUP

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Italy

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from this website https://www.chiesi.com/en/chiesi-clinical-trial-data-request-portal/ in accordance with the Chiesi Farmaceutici clinical trial data request process

IPD sharing plan summary
Available on request