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A clinical trial comparing the difference between participants who are frequently monitored for their compliance with their inhaler medication and participants who receive only their routine care in people suffering from asthma or COPD

Submission date
07/06/2022

Recruitment status
Stopped

Registration date
21/09/2022

Overall study status
Stopped

Last Edited
06/08/2024

Condition category
Respiratory

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
An estimated 65 million people have moderate to severe chronic airway disease worldwide and about 334 million suffer from asthma. One of the most common ways of treating chronic airway diseases is providing patients with inhalers. However, we also know that one of the barriers to the management of chronic airway diseases is making sure that patients maintain good compliance with their medication. One way that we might be able to improve the management of chronic airway diseases is by helping patients to be more compliant with their medication. This trial aims to find out if there is any improvement in managing chronic airway disease (which will be measured by the number of severe exacerbation's people experience) by using a smartphone app and smart inhaler to remind patients when and how often to use their medication. The smartphone app is designed to help with more frequent monitoring of symptoms and people’s compliance with medication use, and it is connected to a smart inhaler which will be used to deliver a medication regime that is tailored to the individual. This will be compared with a group of other individuals who will continue to receive their normal standard routine care.

Who can participate?
Patients aged 18 years and over with clinically diagnosed airway disease (asthma or COPD)

What does the study involve?
Participants will be required to use their own mobile phones devices and to download several apps that are required for the collection of trial data. This may use up mobile data and as such,

participants will be encouraged to use wifi where possible to complete downloads and data entry, however, when this isn't possible and data charges are incurred, data vouchers can be provided to participants as recompense.

Participants are required to attend Primary Care or Hub sites ahead of scheduled video consultation visits for the purpose of having blood samples taken. This may cause some inconvenience but research staff will be booking and facilitating the booking of these appointments on behalf of participants.

What are the possible benefits and risks of participating?
The trial medications may cause some adverse side effects. The medications are licensed and have favourable safety profiles. Participants will be informed of the potential side effects at the screening visit and will be reviewed frequently throughout the trial where adverse events can be managed accordingly.

Where is the study run from?
University of Leicester (UK)

When is the study starting and how long is it expected to run for?
June 2022 to August 2025

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
Dr Neil Greening (Principal investigator) (UK)
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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-005934-41

Integrated Research Application System (IRAS)
1004465

Central Portfolio Management System (CPMS)
53428

Protocol serial number
0842

Study information

Scientific Title
A pragmatic, off-label, randomised controlled trial of variable inhaled corticosteroid dosing by blood eosinophil level and medication adherence digital evaluation in airways disease

Acronym
VIDEO-MADE

Study objectives

1. To compare therate ofannualised airway disease exacerbations over24 weeks,between the biomarker intervention arm and the standard of care arm
2. To compare the following outcome measures between the biomarker intervention arm and the usual care arm:
2.1. Pre-bronchodilator lung function
2.2. Compliance with the biomarker algorithm based treatment advisories
2.3. Health related quality of life
2.4. Annualised rate of moderate-severe exacerbation events

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 22/NE/0110

Primary study design
Interventional

Study design
Randomized controlled single-blind parallel-group

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Chronic airway disease (Asthma or COPD)

Interventions
Trial participants will enter the study on their established ICS/LABA ± LAMA therapy prior to trial entry (routine inhaled therapy)
Routine inhaled therapy will be replaced with study treatments, Relvar®Ellipta® (fluticasone furoate vilanterol) ± Incruse®Ellipta® (umeclidinium bromide, with umeclidinium as a fixed dose additional therapy) at an equivalent ICS dose based upon a reported therapeutic index study.

1. Biomarker intervention arm
1.1. Titration of corticosteroid component of study inhaler depending on blood eosinophil level and measured adherence level. Dose titration is to be delivered based on eosinophil count only if the adherence level is >75%. Adherence intervention will be delivered based on calibrated adherence to study advisory irrespective of blood eosinophil level.
1.2. Dose titration options (according to a pre-specified biomarker algorithm):
1.2.1. Relvar®Ellipta® 92/22 (fluticasone furoate/vilanterol)
1.2.2. Relvar®Ellipta®® 184/22 (fluticasone furoate/vilanterol)
1.2.3. Anoro@ Ellipta@ (umeclidinium/vilanterol) for persistently biomarker low adherent patients with COPD only

1.3. Pre-defined study adherence cut-off thresholds and interventions (platforms supported by Propeller Health Ltd (monitoring) and Atom5 TM (intervention)).
1.3.1. Low Adherence rate (video consultation-based behavioural interventions and Atom5TM

App-based push reminders only
1.3.2. Moderate and good Adherence rate (>50% Adherence) – App-based push reminders only and no intensive intervention

2. Standard of care arm
2.1. Trial participants will switch to therapeutic dose equivalent Relvar®Ellipta® ±Incruse®Ellipta®(umeclidinium as a fixed dose additional therapy) similar to the intervention arm.
2.1. Participants will undergo routine standard of care and follow-up by their usual care provider without further dose titration.
Propeller Health platform will support passive monitoring of inhaler adherence which will be continued until the study endpoint.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Fluticasone furoate/vilanterol, umeclidinium bromide, umeclidinium/vilanterol

Primary outcome(s)
1. Annualised rate of airway disease exacerbations from baseline to 24 weeks, with exacerbations defined as:

1.1. Mild exacerbations (any one of):
1.1.1. Nocturnal awakening(s) on at least 2 nights
1.1.2. Increase in short-acting beta agonist (SABA) use for at least 2 nights
1.1.3. ≥20% decrease in peak expiratory flow on at least 2 nights compared to the optimal run-in peak flow reading
1.1.4. ≥20% decrease in FEV1 compared to optimal run-in FEV1 reading
1.1.5. A visit to the emergency department (ED)/trial team for increased symptoms but not requiring additional systemic corticosteroids.

1.2. Moderate-to-severe exacerbation (any one of):
1.2.1. Use of systemic corticosteroids ±antibiotics, or an increase from a stablemaintenance dose, for at least 3 days. A period of 7 days or more between additional corticosteroids will be defined as a separate event
1.2.3. An episode of hospitalization or ED (emergency department) visit because of increased airways disease symptoms, requiring systemic corticosteroids ± antibiotics

Exacerbations will be captured via the electronic symptom diary supported by digital platform Atom5 and Nuvoair, with data collected three times per week to allow monitoring mild exacerbation events.

2. Annualised rate of all airway disease exacerbations from baseline visit to the study endpoint (24 weeks)

Key secondary outcome(s)

1. Secondary outcome measures from baseline (week 0) to week 24:
1.1. Pre-bronchodilator Forced Expiratory Volume in 1 second (FEV1) and FEV1/FVC measured at study visits (weeks0,12 & 24)
1.2. Compliance with biomarker algorithm-based treatment advisories during the trial (proportion of days in the month that participants adhere to algorithm-based treatment advisories over 24 weeks). Electronically monitored adherence profile (weeks 0, 4, 8,12 & 24)
1.3. St George's Respiratory Questionnaire score (SGRQ)(weeks 0, 12 & 24)
1.4. Annualised rate of moderate to severe exacerbationeventsrequiringoral corticosteroids or antibiotics

2. Exploratory (Clinical biomarkers):
To compare the following outcome measures between the biomarker intervention arm and the standard of care arm:
2.1. Additional exacerbation outcomes:
2.1.1. Time to first moderate-severe exacerbation
2.1.2. Hospital or Emergency Department (ED) admissions due to exacerbations of airway disease
2.2. Biomarkers:
2.2.1. Change in blood eosinophil counts (weeks 0, 12 & 24)
2.3. Symptom questionnaires (Comparison of change over 24 weeks and responder analysis)
2.3.1. COPD Assessment Tool (CAT) for COPD participants
2.3.2. Asthma Control Test Score (ACT) for Asthma patients
2.3.3. Extended MRC dyspnoea score (eMRC) for participants with both asthma and COPD

3. Exploratory (Digital biomarkers):
The following digital biomarkers will be collected and assessed as exploratory analyses at Imperial College, London
3.1. Composite Exacerbation Endpoints:
Analysis of thrice weekly study acquired PEFR/FEV1, Reliever use and symptom scores with a view to deriving composite exacerbation endpoint measurements using threshold and slope-based indices. (weeks 0-12, 13-24 & 0-24)
3.2. Cough biomarker analysis (Nuvoair data):
3.2.1. Cough counts (weeks 0-12, 13-24 & 0-24)
3.2.2. Cough sound biomarkers (including frequency - median (range) and amplitude) (weeks 0-12, 13-24 & 0-24)
3.3. Physical activity monitoring biomarkers (Fitbit data):
3.3.1. Daily step count (weeks 0-12, 13-24 & 0-24)
3.3.2. Mean and standard deviation of daily heart rate (weeks 0-12, 13-24 & 0-24) Mean and standard deviation of daily energy expenditure (weeks 0-12, 13-24 & 0-24)
3.3.3. Sleep duration (weeks 0-12, 13-24 & 0-24)
3.4. Causal inference analyses using complier average causal effect (CACE) modelling of study adherence data and exacerbation events, with a view to understanding the impact of temporal variations in adherence to inhaled therapy and mild, moderate-severe, exacerbations.

4. Biobanking at stable disease state (with optional consent):
4.1. Collection of the following biological samples at the screening visit (week -34 to -22) and week 24
4.1.1. Blood (DNA PAXgene)
4.1.2. Urine
4.1.3. Serum
4.1.4. Plasma
4.1.5. Nasopharyngeal swab

5. Exacerbation profiling Sub-study (Optional)
A subgroup of trial participants (n = 100 participants, with 50 participants from each trial arm) will be analysed in greater depth if they report a moderate-severe exacerbation event.
Trial participants will be asked to report to their local trial site, should they require oral steroids or antibiotics for an exacerbation, preferably prior to initiating treatment
5.1. The following samples will be collected at these exacerbation visits:
5.1.1. Blood tests (FBC, C-Reactive Protein)
5.1.2. Spontaneous Sputum samples
5.1.3. Plasma
5.1.4. Nasopharyngeal swabs
5.1.5. Urine

Completion date
01/08/2025

Reason abandoned (if study stopped)
Lack of funding/sponsorship

Eligibility

Key inclusion criteria
1. Clinically diagnosed airway disease (asthma or COPD)
2. Blood eosinophil count of ≥ 0.2 x 109/L either at the clinic visit or any one time in the preceding 24 months
3. History of “Exacerbation prone airway disease” (defined as 2 or more exacerbations requiring oral corticosteroids and or antibiotics within 12 months of initial pre-screening review)
4. Male and female patients aged 18 years and over
5. Willing and able to consent to participate in trial
6. Able to use a smartphone device and comply with biomarker guided protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Key exclusion criteria
1. Unable to give informed consent
2. Unable to use a smartphone device and or comply with biomarker guided protocol
3. Absence of eosinophilia (defined as persistently < 0.2 x 109 cells/L withing the last 24 months)
4. History of unstable or severe cardiac, hepatic, thyrotoxicosis, or renal disease, or other

medically significant illness which the investigator believes would be a contraindication to study participation
5. Current or within the last 6 months (or maximum relevant wash out period, whichever is longer), participation in an investigational medicinal product (IMP) or device trial at the time of screening
6. History of long QT syndrome or whose QTcF interval (Fridericia's) is prolonged >450 msec at screening or baseline
7. History of previous hospital admission as pneumoniaa (with radiological lung changes) prior to 12 months of study screening
8. History of human immunodeficiency virus (HIV) or hepatitis B or C
9. History of active Malignancy in any organ system (diagnosis within last 12 months or ongoing active cancer treatment such as chemotherapy, radiotherapy, or immunotherapy
10. Patients whose treatment is considered palliative (life expectancy < 6 months).
11. Pregnancy/lactating or intends to become pregnant during the study period where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test in urine or serum
12. Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, who are not able to use effective methods of contraception during dosing of trial treatment and for a minimum of 1 month after their last treatment
13. Patients with clinically significant laboratory abnormalities (not associated with the study indication) at screening including (but not limited to):
13.1. AST or ALT >2.0x upper limit of normal (ULN)
13.2. Total bilirubin >1.3 X ULN at screening (except for patients with Gilberts syndrome where suitability for inclusion will be left to the discretion of the local investigator)

Date of first enrolment
31/07/2022

Date of final enrolment
01/08/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
University of Leicester

ROR
https://ror.org/04h699437

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (GSK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from the trial contact Dr Neil Greening (Principal investigator), neil.greening@leicester.ac.uk

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No