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Efficacy and safety of GSK3923868 inhalation powder, during experimental human rhinovirus infection in participants with asthma

Submission date 03/03/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 13/05/2022	**Overall study status** Completed	
Last Edited 11/06/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
GlaxoSmithKline (GSK) is developing a new drug (GSK3923868) for the treatment of human rhinovirus (HRV), the most common cause of the common cold. The symptoms following HRV infection are generally limited to runny nose, sore throat and sneezing (i.e. the upper respiratory tract). However, in patients with long-term lung conditions such as chronic obstructive pulmonary disease (COPD) and asthma, HRV infection can lead to sudden worsening of disease symptoms (exacerbations) through infection of the lung itself. Exacerbations can result in serious illness that can cause hospitalisation or even death.
Currently, there are no available treatments or vaccines for HRV, other than medicines that help to treat cold symptoms. Our study drug works by disrupting the process the virus uses to reproduce itself, which may help improve the immune system's ability to fight off lung infections. If the study drug works, it will provide a good treatment option for patients with COPD and asthma to prevent exacerbations.
This study will also assess the safety of the study drug, levels of the study drug in the blood and biomarkers of HRV infection.

Who can participate?
Adults between 18 and 65 years, with a diagnosis of asthma

What does the study involve?
This study has two parts, Parts A and B. The main aim of this study is to assess how well the study drug reduces lung symptoms in participants with asthma.
Part A Cohort 1 will assess how well the study drug works at preventing lung symptoms after experimental HRV infection (i.e. therapeutic treatment). If the study drug works well in this setting, then the time between experimental infection and taking the study drug will be increased (Cohort 2). If the study drug doesn't show enough impact on symptoms in Cohort 1, then the study will progress to Part B (Cohort 3). Part B will assess how taking the study drug prevents lung symptoms before experimental HRV infection (i.e. prophylactic treatment).

What are the possible benefits and risks of participating?
Benefits:
None
Risks:
This study will be the first administration of GSK3923868 to research participants during an HRV infection and has been designed to assess the efficacy, safety, tolerability, PK and PD of the study intervention. GSK3923868 has been administered to human subjects, but due to the lack of experience in human subjects to date, there is no information available about the relationship of adverse events to the administration of GSK3923868.
The research participants will be infected with HRV-16 (common cold) and this could lead to the development of common cold symptoms. The participants will be closely monitored by physicians and nurses in case of any discomfort and medication in case of any discomfort and rescue inhalers will be available in the event of an exacerbation. The anticipated symptoms they might experience associated with HRV-16 infection include runny nose, stuffy nose, sneezing, sore throat, coughing, chest tightness, shortness of breath, wheezing and nighttime awakenings. The burden on the participants is that they will be housed in a quarantine unit for 16 days during the clinical trial so their safety and symptoms can be monitored which will include providing virology and blood samples. The stay is aimed to be as comfortable as possible within the quarantine unit with their en-suite room which has entertainment including wifi, TV and gaming console and all meals are catered for.

Where is the study run from?
Not provided at time of registration

When is the study starting and how long is it expected to run for?
February 2022 to April 2024

Who is funding the study?
GlaxoSmithKline Research & Development Limited (UK)

Who is the main contact?
Dr Melissa Bevan, m.bevan@hvivo.com

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Additional identifiers

EudraCT/CTIS number
2021-006640-27

IRAS number
1005333

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
213499, IRAS 1005333

Study information

Scientific Title
A randomised, double-blind, placebo-controlled, repeat dose phase 1b study to assess the efficacy, safety, tolerability, pharmacokinetics and pharmacodynamics of Inhaled GSK3923868 during experimental human rhinovirus infection in participants with asthma

Study objectives
To evaluate the impact of once daily administration of GSK3923868, compared with placebo, on lower respiratory tract symptoms (LRTS), in asthmatics experimentally infected with HRV-16.

To evaluate the impact of once daily administration of GSK3923868, compared with placebo, on symptoms, in asthmatics experimentally infected with HRV-16.

To evaluate the efficacy of once daily administration of GSK3923868, compared with placebo, on lung function in asthmatics experimentally infected with HRV-16.

To assess the safety and tolerability of once daily administration of GSK3923868 in asthmatics experimentally infected with HRV-16

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 11/05/2022, South Central - Hampshire B Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)20 7104 8604; hampshireb.rec@hra.nhs.uk), ref: 22/SC/0083

Study design
Interventional double-blind randomized placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Interventions
In all cohorts, participants will be admitted to the unit on Day -1, will be inoculated with HRV-16 and will remain resident at the unit until discharge. GSK3923868 will be administered as an inhaled powder capsule. During this time efficacy, safety, tolerability, pharmacokinetic (PK) and pharmacodynamic (PD) assessments will be completed. The final follow up will be 7 days after the final dose of GSK3923868.

In Part A Cohorts 1 & 2: 10 days of treatment with GSK3923868 will be initiated after viral inoculation. After the completion of Part A Cohort 1 and interim analysis will be carried out. The results will trigger progression to either Part A Cohort 2 or Part B. In Part B 14 days of treatment with GSK3923868 will be initiated before experimental infection with HRV-16.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Prophylactic treatment

Phase
Phase I

Drug/device/biological/vaccine name(s)
GSK3923868

Primary outcome measure
1. Area under the curve (AUC) for lower respiratory tract symptoms measured using lower respiratory tract symptoms (LRTS) score from time of inoculation to discharge.
2. Lower respiratory tract symptoms (LRTS) score from D-1 up to discharge from quarantine.

Secondary outcome measures
1. Lower respiratory tract symptoms (LRTS) score from D-1 up to discharge.
2. Total upper respiratory tract symptoms (URTS) score from D-1 up to discharge.
3. Spirometry from screening up to follow up.
4. Peak expiratory flow (PEF) from day D-1 to discharge.
5. AEs from Day 1 to follow up
6. Safety laboratory data from screening to follow up
7. Vital signs from screening to follow up
8. ECG 12-lead data from screening to follow up

Overall study start date
28/02/2022

Completion date
09/04/2024

Eligibility

Key inclusion criteria
1. Age between 18 and 65 years of age inclusive, at the time of signing the informed consent.
2. Type of Participant
2.1. A physician diagnosis of asthma, as defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation [Global Initiative for Asthma (GINA), 2021] at least 6 months before Screening.
2.2. The criteria for diagnosis of asthma should be documented in the participant’s source data, including relevant history.

2.3. A screening pre-bronchodilator FEV1 ≥65% predicted normal value.
2.4. Positive Methacholine challenge test, defined as ≥20% fall in FEV1 at a methacholine concentration ≤16 mg/mL, at Screening Visit.
2.5. Positive skin prick test to at least one allergen (e.g. house dust mite, cat dander, grass pollen) at Screening Visit.
2.6. Serology suitable for the challenge virus:
2.7. The serology results obtained from the HRV-16 neutralisation antibody assay suggests that the participant will be susceptible to HRV-16 infection (i.e. they are likely to be infected following inoculation with the challenge virus).
2.8. Participants with controlled asthma, according to Investigator judgement, using short-acting beta agonist (SABA) or intermittent inhaled corticosteroid (ICS) or ICS/long-acting beta agonist (LABA) therapy used as rescue.
3. Body weight at least 50.0 kg (110 lbs) and body mass index (BMI) within the range 18.5 to 34.0 kg/m² (inclusive).
4. Sex
4.1. Males and female participants, as follows:
4.2. Male Participants: No additional requirements.
4.3. Female Participants: A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least one of the following conditions applies:
•Is a woman of non-childbearing potential (WONCBP) as defined in the protocol OR
•Is a woman of childbearing potential (WOCBP) and using an acceptable contraceptive method as described in the protocol during the intervention period and for at least 28 days after inoculation. The investigator should evaluate the potential for contraceptive method failure (e. g. noncompliance, recently initiated in relationship to the first dose of study intervention). A WOCBP must have a negative highly sensitive pregnancy test (urine or serum as required by local regulations) within 48 hours before the first dose of study intervention or Viral Challenge (whichever occurs first).
Note: If a urine test cannot be confirmed as negative (e.g. an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.
5. Capable of giving signed informed consent, which includes compliance with the requirements and restrictions listed in the informed consent form (ICF) and in the protocol

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
68

Total final enrolment
47

Key exclusion criteria
1. Medical Conditions
1.1. Any asthma exacerbation requiring systemic corticosteroids within 8 weeks of admission, or that resulted in overnight hospitalization requiring additional treatment for asthma within 3 months of admission
1.2. A history of life-threatening asthma, defined as any asthma episode that required admission to a high-dependency or intensive therapy unit.
1.3. The presence of concurrent significant pulmonary diseases, other than asthma, including (but not limited to): bronchiectasis, pulmonary fibrosis, bronchopulmonary dysplasia, chronic bronchitis, emphysema, chronic obstructive pulmonary disease, or other significant respiratory abnormalities.
1.4. The presence of other concurrent diseases/abnormalities that, in the opinion of the Investigator, would put the safety of the participant at risk or would confound the interpretation of the results in this study.
1.5. Please Note: participants with a history of resolved mild depression and/or anxiety 1 or more years ago may be included if the patient health questionnaire(PHQ-9) and/or the generalised anxiety disorder questionnaire (GAD-7) is less than or equal to 4 on admission to the clinical unit. Participants with a history of stress-related illness, which is not on-going or requiring current therapy, with good evidence of preceding stressors may also be included based on Investigator's judgement.
1.6. Any significant abnormality altering the anatomy of the nose in a substantial way or nasopharynx that may, in the Investigator's judgement, interfere with the aims of the study.
1.7. Any clinically significant history of epistaxis (large nosebleeds) within the last 3 months of admission and/or history of being hospitalised due to epistaxis on any previous occasion.
1.8. Any nasal or sinus surgery within 3 months of admission.
1.9. Has had any acute illness, including a common cold or other respiratory tract infection, within 6 weeks before admission to the unit.9.Has had any major illness or hospitalisation within 6 months before admission to the unit.10.ALT above 1.1 x upper limit of normal (ULN)
1.10. Lifetime history of anaphylaxis and/or a history of severe allergic reaction or significant intolerance to any food or drug, as assessed by the Investigator.
1.11. Current or chronic history of liver disease or known hepatic or biliary abnormalities (with the exception of Gilbert's syndrome or asymptomatic gallstones).
1.12. QTcF >450 msec on Day -1based on the average of triplicate ECGs.
2. Prior/Concomitant therapy
2.1. Past or intended use of over-the-counter or prescription medication, including (but not limited to) nasal decongestants, cold remedies, herbal and dietary supplements (including St John's Wort; vitamins are allowed) within 5days before the Viral Challenge or first dose of study intervention (whichever occurs first), unless in the opinion of the Investigator and the GSK Medical Monitor, the medication will not interfere with the study objectives or compromise participant safety.
2.2. Evidence of vaccinations within the 4 weeks prior to the planned date of Viral Challenge or first dosing with IMP (whichever occurs first).
2.3. Intention to receive any vaccination(s) before the last day of Follow Up.
3. Prior/Concomitant clinical study experience
3.1. Participation in this study would result in loss of blood or blood products in excess of 500mL within 56 days.
3.2. Exposure to more than 4 new chemical entities within 12 months before the first dosing day.
3.3. Current enrolment or past participation in a clinical trial and has received an investigational

product within the following time period before the first dosing day in this study: 30 days, 5 half-lives or twice the duration of the biological effect of the investigational product (whichever is longer).
3.4. Prior inoculation with a virus from the same virus-family as the Challenge Virus.
3.5. Prior participation in another Human Viral Challenge study with a respiratory virus in the preceding 12 months.
4. Diagnostic Assessments
4.1. Positive pathogen screen for respiratory tract infection including COVID-19 within 5 days of first dose or viral inoculation (whichever occurs first).
4.2. Presence of hepatitis B surface antigen (HBsAg) at Screening or within 3 months prior to first dose of study intervention.
4.3. Positive hepatitis C antibody test result at Screening or within 3 months prior to first dose of study intervention.

Date of first enrolment
01/06/2022

Date of final enrolment
25/03/2024

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
hVIVO Services Ltd
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline Research & Development Limited

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Submission to regulatory authorities
GSK online system enables researchers to request access to anonymised patient level data that sit behind the results of clinical trials. It is hoped that sharing these data with researchers will help to further scientific understanding and improve patient care. This system will allow researchers to examine the study details more closely, do their own analyses and learn more about medicines and how they can best be used.

Intention to publish date
09/04/2025

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No