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A study to evaluate the safety, tolerability, and efficacy of galicaftor/navocaftor/ABBV-119 combination therapy in subjects with cystic fibrosis

Submission date
28/01/2022

Recruitment status
Stopped

Registration date
07/03/2022

Overall study status
Stopped

Last Edited
05/01/2024

Condition category
Nutritional, Metabolic, Endocrine

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

Plain English summary of protocol

Background and study aims
Cystic Fibrosis (CF) is a rare, life-threatening, genetic disease that affects the lungs and digestive system, significantly impairing the quality of life, with those affected having a median age of death at 40. The main objective of this study is to assess how safe and effective is the combination therapy of galicaftor/navocaftor/ABBV-119 in adult participants with CF

Who can participate?
Patients with CF, and the F508del CFTR mutation (the most common CF gene mutation)

What does the study involve?
Galicaftor/navocaftor/ABBV-119 combination therapy is being developed as an investigational drug for the treatment of CF. Study doctors place participants in 1 of the 4 groups, called treatment arms. Each group receives a different treatment. Around 90 adult participants with a diagnosis of CF will be enrolled in the study around approximately 35 sites worldwide. Participants in arm 1 will receive oral capsules of galicaftor/navocaftor dual combination for 28 days followed by galicaftor/navocaftor/ABBV-119 triple combination for 28 days. Participants in arms 2 and 3 will receive the galicaftor/navocaftor/ABBV-119 triple combination or placebo for 28 days. Participants in arm 4 will receive galicaftor/navocaftor/ABBV-119 triple combination therapy for 28 days. For all study arms, galicaftor, navocaftor, will be given once daily and ABBV-119 twice a day.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
ABBV-119 A small number of healthy volunteers who received ABBV-119 for up to 14 days had elevated blood levels of liver enzymes (ALT and AST), a possible sign of injury to the liver. The volunteers did not have any complaints along with these abnormal blood tests. The tests

returned to normal or near normal levels within the next 2 weeks. There could be a risk of side effects related to sunlight exposure or ultraviolet (UV) light exposure. It is not known whether exposure to sunlight might lead to skin irritation or cause one to break out in a rash or sunburn. If possible, patients should avoid direct exposure to the sun for long periods of time while participating in this clinical study. Protective clothing and sunglasses as well as sunscreen (SPF 30 or higher) should be used if exposed to sunlight. In addition, patients should not expose themselves to sun lamps, tanning booths, or tanning beds.
Most common side effects of the combination of galicaftor and navocaftor: Headache/Fatigue /Back pain/Constipation/Dry lips/Decreased urination/Nausea/Rash
Risks related to Study Procedures:
Blood Testing: may cause pain, bleeding, and/or bruising
Sweat collection: may cause tingling of the skin. The sticky pads may result in “irritation” of the skin. There is a remote possibility of a burn due to the test.
Lung Function Testing: may feel the need to cough, or feel a bit short of breath and lightheaded
5-day washout may lead to withdrawal symptoms

Where is the study run from?
St James's University Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2022 to December 2022

Who is funding the study?
AbbVie Ltd (UK)

Who is the main contact?
Dr Daniel Peckham, daniel.peckham@nhs.net

Contact information

Type(s)
Principal Investigator

Contact name
Dr Daniel Peckham

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Additional identifiers

EudraCT/CTIS number
2020-005805-25

IRAS number
1004477

ClinicalTrials.gov number
NCT04853368

Secondary identifying numbers
M19-771, IRAS 1004477, CPMS 51119

Study information

Scientific Title
A phase 2 study of galicaftor/navocaftor/ABBV-119 combination therapy in subjects with cystic fibrosis who are homozygous or heterozygous for the F508del mutation

Study objectives
The primary objective is to evaluate the safety, tolerability, and efficacy for galicaftor/navocaftor /ABBV-119 combination therapy in adult subjects with CF who are homozygous or heterozygous for the F508del mutation.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, HRA Fast Track REC, ref: 22/FT/0001

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Cystic Fibrosis

Interventions
Study doctors place participants in 1 of the 4 groups, called treatment arms. Each group receives a different treatment. Around 90 adult participants with a diagnosis of CF will be enrolled in the study at approximately 35 sites worldwide.

Participants in arm 1 will receive oral capsules of galicaftor/navocaftor dual combination for 28 days followed by galicaftor/navocaftor/ABBV-119 triple combination for 28 days.
Participants in arms 2 and 3 will receive the galicaftor/navocaftor/ABBV-119 triple combination or placebo for 28 days.
Participants in arm 4 will receive galicaftor/navocaftor/ABBV-119 triple combination therapy for 28 days.
For all study arms, galicaftor, navocaftor, will be given once daily and ABBV-119 twice a day.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
galicaftor, navocaftor, ABBV-119

Primary outcome measure
The primary endpoint is the absolute change from Baseline through Day 29 in percent predicted forced expiratory volume in 1 second (ppFEV1) measured using spirometry

Secondary outcome measures
Measured using spirometry unless noted otherwise:
1. Absolute change from Baseline through Day 29 in Sweat Chloride (SwCl) measured using sweat samples
2. Absolute change from Baseline through Day 29 in forced vital capacity [FVC]
3. Absolute change from Baseline through Day 29 in forced expiratory flow at mid-lung capacity [FEF25-75]
4. Relative changes from Baseline through Day 29 in ppFEV1
5. Relative changes from Baseline through Day 29 in FVC
6. Relative changes from Baseline through Day 29 in FEF25-75
7. Absolute change in CF Questionnaire-Revised (CFQ-R) respiratory domain score from Baseline through Day 29

Overall study start date
07/01/2022

Completion date
16/12/2022

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria
1. Confirmed clinical diagnosis of CF, and genotype homozygous for the F508del CFTR mutation for Cohort 1 and Cohort 3, heterozygous for F508del CFTR mutation and a minimal function mutation for Cohort 2 and Cohort 3.
2. ppFEV1 ≥40% and ≤90% of predicted normal for age, gender, and height (Global Lung

Function Initiative [GLI] equations) at Screening.
3. No clinically significant laboratory values at Screening that would pose undue risk for the subject or interfere with safety assessments (per the investigator).
4. Absence of clinically significant abnormality detected on ECG regarding rate, rhythm, or conduction (e.g., QT interval corrected for heart rate using Fridericia's formula [QTcF] should be < 450 msec for males and <460 msec for females).
5. Stable pulmonary status, i.e., no respiratory infections or exacerbations requiring a change in therapy (including antimicrobials) or causing an acute decline in ppFEV1 of >10% from usual ppFEV1 level within 4 weeks.
6. SwCl at screening visit must be ≥60 mmol/L for Cohort 1 and Cohort 2, and this criterion does not apply to Cohort 3.
7. No history of diseases aggravated or triggered by ultraviolet radiation and no history of abnormal reaction photosensitivity or photoallergy to sunlight, or artificial source of intense light, especially ultraviolet light.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
90

Key exclusion criteria
1. Cirrhosis with or without portal hypertension (e.g., splenomegaly, esophageal varices) or history of clinically significant liver disease
2. History of malignancy within past 5 years (except for excised basal cell carcinoma of the skin with no recurrence, or treated carcinoma in situ of the cervix with no recurrence)
3. Recent (within the past 6 months) history of drug or alcohol abuse that might preclude adherence to the protocol, in the opinion of the investigator
4. Smoking or vaping tobacco or cannabis products within 6 months before Screening
5. History of solid organ or hematopoietic transplantation
6. History of known sensitivity to any component of the study drug
7. Need for supplemental oxygen while awake, or >2 L/minute while sleeping.
8. Evidence of active SARS-CoV-2 infection. If a subject has signs/symptoms suggestive of SARS CoV-2 infection, they should undergo molecular (e.g., polymerase chain reaction [PCR]) testing to rule out SARS-CoV-2 infection.

Date of first enrolment
28/07/2021

Date of final enrolment
16/12/2022

Locations

Countries of recruitment

Belgium

Canada

England

France

Hungary

Netherlands

Puerto Rico

Scotland

Serbia

Slovakia

Spain

United Kingdom

Study participating centre
The Adult Cystic Fibrosis Centre
Royal Papworth Hospital NHS FT
Papworth Road
Cambridge
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Study participating centre
Queen Elizabeth University Hospital
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Study participating centre
All Wales Adult Cystic Fibrosis Centre
Cardiff and Vale University Health Board
Penlan Road
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Study participating centre
King's College Hospital
Denmark Hill
London
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SE5 9RS

Study participating centre
Royal Brompton Hospital
Sydney Street
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SW3 6NP

Study participating centre
Manchester Adult Cystic Fibrosis Centre
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Study participating centre
Southampton General Hospital
Tremona Road
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Sponsor information

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Sponsor type
Industry

Website
http://www.abbvie.co.uk/

ROR
https://ror.org/04tnbfn25

Funder(s)

Funder type
Industry

Funder Name
AbbVie

Alternative Name(s)
AbbVie Inc., AbbVie U.S., AbbVie US, Allergan

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Submission to regulatory authorities
When study results become available, the investigator brochure for the study IMP will be

updated to inform the study investigators of the safety and efficacy results from the study. Once the final study report becomes available, study results will be uploaded to Clinicaltrials.gov. Patients and members of the community can gain access to the published material.

Intention to publish date
16/12/2023

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available.

IPD sharing plan summary
Not expected to be made available