ISRCTN15406513 https://doi.org/10.1186/ISRCTN15406513

A study to evaluate safety and processing by body of GDC-6988 in healthy adults receiving albuterol as a pretreatment medication

Submission date	Recruitment status	[X] Prospectively registered
28/06/2022	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
07/07/2022	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
07/07/2022	Other	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims:
Cystic fibrosis is a genetic disorder that mainly affects the lungs, digestive system, and other organs in the body. Cystic fibrosis is caused by the change (mutation) of a gene which leads to dysfunction in the cells that produce mucus. Mucus is a fluidic substance which helps lubricate and protects the linings of organs and tissues in the human body. This genetic dysregulation leads to build-up of thick sticky mucus which clogs the tubes, ducts, or passageways of organs and in turn leading to severe damage to organs in the form of fluid filled sacs (cysts) or scar tissue (fibrosis) formation.

The aim of this study is to test study drug GDC-6988 designed to treat cystic fibrosis at different dose levels in healthy participants to find out if it is safe. The study also looks to see how the study drug is being processed by the human body. GDC-6988 is an experimental drug, which means health authorities have not approved GDC-6988 for the treatment of cystic fibrosis or any other disease.

Who can participate?
Healthy volunteers aged between 18 to 55 years of age.

What does the study involve?
Participants will need to be a part of this study for about 70 days. This study will have three parts:
1. A screening visit, where certain tests would be done to determine if the participant is eligible to take part in the study.
2. Treatment period, where eligible participants will be enrolled and will receive an inhaled dose of GDC-6988 or a medication that has no active ingredient (placebo). The treatment (GDC-6988 or placebo) will be decided by chance (like tossing a coin). The participants will have a one in five chance of getting placebo. Treatment will be administered twice a day (about every 12 hours) over about 15 minutes for 14 days, with each dose given using a device called a dry powder inhaler (DPI). On Days 8-14, participants will also receive an inhaled dose of salbutamol given using a DPI, about 15 minutes before each dose of study drug. Participants will be required to

check in to the clinic 2 days before receiving the study drug and will be required to stay at the clinic for about 16 nights.
3. A follow-up period during which participants will have to return to the clinic for two follow-up visits (each lasting about 1-2 hours): one visit about 3 days after the participants check out and another visit about 28 days later.

What are the possible benefits and risks of participating?
Participants will not receive any direct medical benefit, but the information gained from this study may help other people with cystic fibrosis in the future.
Participants may have side effects from the drug (GDC-6988), salbutamol, or procedures used in this study. These can be mild to severe and even life-threatening, and they can vary from person to person. The potential side effects associated with GDC-6988, salbutamol, and other procedures are listed below:

Risks associated with GDC-6988:
GDC-6988 has had limited testing in humans. There are no known side effects of this drug at this point in time. Potential side effects include difficulty in breathing and chest tightness.

Risks associated with Salbutamol:
Side effects associated with salbutamol use include elevated heart rate, shakiness, taste disturbances, and nausea/upset stomach.

Risks associated with the study procedures:
Blood sampling: Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some participants might experience dizziness, fainting, or an upset stomach when their blood is drawn.

There may be a risk in exposing an unborn child to the study drug, and all risks are not known at this time. Women and men must take precautions to avoid exposing an unborn child to the study drug. Participants who are pregnant, become pregnant or are currently breastfeeding cannot take part in this study.

Where is the study run from?
F. Hoffmann-La Roche Ltd (USA)

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

Who is funding the study?
F. Hoffmann-La Roche Ltd (USA)

Who is the main contact?
Dr Nand Singh
global-roche-genentech-trials@gene.com

Contact information

Type(s)
Public

Contact name

Dr Nand Singh

Contact details
Mere Way
Ruddington Fields
Ruddington
Nottingham
United Kingdom
NG11 6JS
+44 (0)330 3031000
global-roche-genentech-trials@gene.com

Additional identifiers

Clinical Trials Information System (CTIS)
2022-000455-36

Protocol serial number
GB43838

Study information

Scientific Title
A phase Ib, randomized, double-blind, placebo-controlled, single-center study to evaluate the safety and pharmacokinetics of multiple ascending doses of GDC-6988 with and without albuterol pretreatment in healthy adult subjects

Study objectives
The purpose of the study is to test GDC-6988 at different doses and to find out if it is safe and to understand the way the human body processes the drug.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, London - Riverside Research Ethics Committee (Level 3 Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, UK; +44 02071048044; riverside.rec@hra.nhs.uk)

Study design
Phase Ib randomized double-blind placebo-controlled single-centre, dose-escalation interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Safety and pharmacokinetics of multiple ascending doses of GDC-6988 with and without albuterol pretreatment in healthy adult subjects

Interventions

Participants in this study will receive a multiple ascending dose of GDC-6988 or placebo as follows:

Cohort A: Participants will receive 11.2 milligrams (mg) of GDC-6988 (or placebo) as dry powder inhalation, administered using the Smart Dry Powder Inhaler (DPI), twice a day (BID) for 14 days. Starting on Day 8, participants will receive pre-treatment dose of salbutamol up to Day 14.

Cohort B: Participants will receive 22.4 mg of GDC-6988 (or placebo) as dry powder inhalation, administered using DPI, BID for 14 days. Starting on Day 8, participants will receive pre-treatment dose of salbutamol up to Day 14.

Cohort C: Participants will receive 42 mg of GDC-6988 (or placebo) as dry powder inhalation, administered using DPI, BID for 14 days. Starting on Day 8, participants will receive pre-treatment dose of salbutamol up to Day 14.

Cohort D (optional cohort): Participants will receive GDC-6988 (dose TBD) or placebo as dry powder inhalation, administered using DPI, BID for 14 days. Starting on Day 8, participants will receive pre-treatment dose of salbutamol up to Day 14.

Participants will be randomised according to the master randomization list. The objective of the randomisation method is to define the TAI (Treatment Assignment Information) datasets based on the protocol. The Statistician is accountable for this step. The statistician will review the protocol and reach out to relevant personnel as required to identify the TAI datasets. The statistician will complete Roche's internal form, and send a copy to the TAI Gatekeeper (internal role within data management and separate from the study team), and other form recipients for use during the clinical trial and archive the form to the study TMF. The statistician will inform the Study Lead that the TAI datasets have been defined before the enrollment of the first subject.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

GDC-6988

Primary outcome(s)

1. Percentage of participants with adverse events (AEs) and severity of AEs determined according to Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Paediatric Adverse Events (HHS 2017) from Day 1 up to 28 days after the final dose of study drug (up to approximately 42 days)
2. Percentage of participants with vital signs abnormalities as assessed by measuring respiratory rate, pulse rate, peripheral oxygen saturation, systolic and diastolic blood pressure and temperature from screening up to 28 days after the final dose of study drug (up to approximately 42 days)

3. Percentage of participants with laboratory test abnormalities measured using biological samples collected from screening up to 28 days after the final dose of study drug (up to approximately 42 days)
4. Percentage of participants with spirometry abnormalities measured using a spirometer from screening up to 28 days after the final dose of study drug (up to approximately 42 days)
5. Percentage of participants with oscillometry abnormalities measured using forced oscillometry technique (FOT) from Day 1 up to 28 days after the final dose of study drug (up to approximately 42 days)
6. Percentage of participants with electrocardiogram (ECG) abnormalities measured using 12-Lead ECG recordings from screening up to 28 days after the final dose of study drug (up to approximately 42 days)
7. Percentage of participants with spirometry abnormalities after salbutamol (albuterol) pretreatment measured using a spirometer from Day 8 up to 28 days after the final dose of study drug (up to approximately 42 days)
8. Percentage of participants with oscillometry abnormalities after salbutamol (albuterol) pretreatment measured using FOT from Day 8 up to 28 days after the final dose of study drug (up to approximately 42 days)

Key secondary outcome(s))
1. Plasma concentration of GDC-6988 measured from blood samples taken at specific timepoints pre-dose and post-dose from Day 1 up to 28 days after the final dose of study drug (up to approximately 42 days)
2. Percentage of participants with device deficiencies measured based on the ISO 14155:2020, device deficiency definition from Day 1 up to 28 days after the final dose of study drug (up to approximately 42 days)
3. Relationship between GDC-6988 exposure and AEs determined according to DAIDS Table for Grading the Severity of Adult and Paediatric Adverse Events (HHS 2017) from Day 1 up to 28 days after the final dose of study drug (up to approximately 42 days)

Completion date
19/12/2022

Eligibility

Key inclusion criteria
1. Age 18 - 55 years at time of signing Informed Consent Form
2. Body mass index of 18 - 32 kilograms per square metre (kg/m²) at screening
3. Body temperature of 35°C - 37.5°C at screening and at Day-1
4. Systolic blood pressure of 90 - 150 millimetres of mercury (mmHg) and diastolic blood pressure of 50 - 95 mmHg at screening and at Day-1. Blood pressure should be measured while the participant is in a seated position.
5. Forced expiratory volume in 1 second (FEV1) >80% of predicted at screening and at Day-1
6. Forced vital capacity (FVC) >2.0 L by spirometry at screening

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group

Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Pregnancy or breastfeeding, or intention of becoming pregnant during the study or within 28 days after the final dose of study drug
2. Treatment with investigational therapy (or blinded comparator) within 90 days or 5 drug elimination half-lives, whichever is longer, prior to initiation of study drug
3. Treatment with any immunosuppressive medication within 28 days or 5 drug elimination half-lives, whichever is longer, prior to initiation of study drug
4. Treatment with an herbal or homoeopathic remedy within 14 days or 5 drug elimination half-lives (whichever is longer) prior to initiation of study drug
5. Treatment with any vaccine within 14 days prior to initiation of study drug or a scheduled vaccination during study period (through the follow-up/early termination visit)
6. Positive for tuberculosis (TB) during screening or within 3 months prior to screening, defined as a positive QuantiFERON®-TB Gold test (QFT)
7. Positive human immunodeficiency virus (HIV) test at screening
8. Positive hepatitis B surface antigen (HBsAg) test at screening
9. Positive hepatitis C virus (HCV) antibody test at screening
10. Receipt of blood products within 120 days prior to screening
11. Hospitalisation within 28 days prior to initiation of study drug
12. Anticipation of need for a surgical procedure during the study
13. Infection requiring oral or intravenous (IV) antibiotics within 28 days prior to screening or any evidence of current infection (e.g., bacterial, viral, fungal)
14. Upper or lower respiratory tract infection within 2 weeks prior to initiation of study drug
15. Documented physician-diagnosed asthma for at least 12 months prior to screening
16. Post-bronchodilator reversibility of FEV1 (litres) ≥12% and ≥200 mL at screening
17. Any medical condition or abnormal clinical laboratory finding that, in the investigator's judgement, would preclude the participant's safe participation in and completion of the study or could affect the interpretation of the results
18. History of malignancy within 5 years prior to screening, except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma, or Stage I uterine cancer
19. History of any significant drug or food allergy (e.g., allergic reactions that resulted in anaphylaxis or hepatotoxicity)
20. History of symptomatic bradycardia
21. History of ataxia or condition associated with ataxia
22. Abnormally low total lung capacity, defined as <80% of predicted for participants of European descent or <75% of predicted for participants of non-European descent, at screening
23. Diffusion capacity of the lung for carbon monoxide, defined as <75% of predicted for participants of European descent or <70% of predicted for participants of non-European descent, at screening
24. Glomerular filtration rate <80 millilitres per minute (mL/min)/1.73 square metre (m^2) as calculated through use of the Chronic Kidney Disease Epidemiology Collaboration equation. Participants with a glomerular filtration rate ≥80 mL/min/1.73 m² and <90 mL/min/1.73 m² are eligible only if have confirmed cystatin C value below upper limit of normal (ULN)

Date of first enrolment
01/08/2022

Date of final enrolment
02/12/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences
Trent House
Mere Way
Ruddington Fields Business Park
Ruddington
Nottingham
United Kingdom
NG11 6JS

Sponsor information

Organisation
F. Hoffmann-La Roche Ltd

Funder(s)

Funder type
Industry

Funder Name
F. Hoffmann-La Roche

Alternative Name(s)
Hoffman-La Roche, F. Hoffmann-La Roche Ltd.

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
Switzerland

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to participant-level data not being a regulatory requirement.

IPD sharing plan summary
Not expected to be made available