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A blinded study in healthy volunteers to evaluate the safety of the test medicine and compare how the test medicine behaves when the dosage is increased, and when taken alone or alongside salbutamol (albuterol)

Submission date
19/07/2022

Recruitment status
No longer recruiting

Registration date
09/08/2022

Overall study status
Completed

Last Edited
06/01/2026

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The Sponsor is developing the test medicine, GDC-6988, for the potential treatment of cystic fibrosis (CF). CF is a genetic disorder, in which the lungs and digestive system get clogged with mucus and can be dangerous and ultimately lead to death. There are treatments available to manage CF, but there is currently no known cure. GDC-6988 increases the activity of the chloride channels in your airways, which help regulate how wet mucus in the airways is. These channels do not work correctly for people with CF, and this leads to a build-up of thick mucus that more readily sticks to the walls of the airways, which can lead to blockages that cause lung damage and respiratory infections, such as pneumonia. This single-part healthy volunteer study will try to evaluate the safety of GDC-6988 and compare how GDC-6988 behaves when the dose is increased, and when taken alone or alongside salbutamol, which is an approved medicine that relaxes the muscles of the airways into the lungs, making it easier to breathe.

Who can participate?
Healthy volunteers aged between 18 and 55 years

What does the study involve?
Participants will be divided in up to five cohorts of 10 volunteers. Cohorts 4 and 5 are optional. They will receive an inhaled dose of up to 42.0 mg of GDC-6988 or placebo (dummy medicine) twice a day from Day 1 to Day 14. They will also receive an inhaled dose of 200 µg salbutamol twice a day from Day 8 to Day 14, and this will be given about 15 minutes before they receive GDC-6988. A smart dry powder inhaler will be used to administer the doses of GDC-6988 or placebo and salbutamol. Participants will be discharged on Day 15 and will return to the clinic on Day 18 and Day 42 for follow-up visits. Their blood and urine will be taken throughout the study for analysis of the test medicine and for their safety. Participants are expected to be involved in this study for approximately 11 weeks from screening to the final follow-up visit.

What are the possible benefits and risks of participating?
This is a healthy volunteer study. Participants will be administered GDC-6988 and salbutamol for research purposes only and it is not intended that the participants will receive any benefit from it. However, the information learned in this study may help future patients. Participants will be compensated for taking part in this research study with an inconvenience allowance.
As this is a Phase I study, the most relevant population is healthy volunteers. It is considered that the risk/benefit evaluation in this study supports the use of healthy male and female volunteers. RO7506811 did not show any evidence of genotoxic activity up to the maximum tolerated dose (1 mg/kg), and as such, female volunteers of child-bearing potential will be enrolled into the study but will be required to follow the strict contraception requirements. Only healthy male and non-pregnant, non-lactating female participants, aged 18 to 55 years are considered suitable for this study. There is always a risk that the stipend in healthy volunteer studies could represent coercion. The time spent in the clinic, travel, inconvenience and other expenses factor in calculating the stipend. Perception of risk is not considered in this calculation. Volunteers may experience side effects from the test medicine. Full information on possible side effects is provided to volunteers. When investigating new medicines there is also a risk of unexpected side effects and occasionally allergic reactions. All volunteers will be closely monitored during the study and safety assessments will be performed at regular intervals. Risks are further mitigated by ensuring that only volunteers who meet all inclusion/exclusion criteria are included and that if the safety of any volunteer represents a concern they will be withdrawn. Blood samples will be collected during the study. Collection of these samples can cause soreness and bruising of the arms but these problems usually clear up within a few days to a few weeks. ECG stickers on volunteers' chests and limbs may cause some local irritation and may be uncomfortable to remove but volunteers will be closely monitored to ensure any local irritation does not continue.

Where is the study run from?
Genentech, Inc. c/o F. Hoffmann-La Roche Ltd (Switzerland)

When is the study starting and how long is it expected to run for?
June 2022 to May 2023

Who is funding the study?
Genentech, Inc. c/o F. Hoffmann-La Roche Ltd (Switzerland)

Who is the main contact?
Trial Information Support Line (TISL), global.clinical_trial_registry@roche.com

Contact information

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Scientific

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

Integrated Research Application System (IRAS)
1005551

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

Acronym
QSC207610

Study objectives
Primary objective:
To evaluate the safety of GDC-6988

Secondary objectives:
1. To characterize the pharmacokinetics (what the test medicine does to the body) of GDC-6988
2. To identify a recommended Phase II dose and regimen for GDC-6988

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, ref: 22/YH/0143

Primary study design
Interventional

Study design
Double-blind randomized placebo-controlled trial

Study type(s)
Other

Health condition(s) or problem(s) studied
Cystic fibrosis (CF)

Interventions
Participants will be randomised to receive a single oral dose of GDC-6988 or placebo twice daily for 14 days (from Day 1 to Day 14).

Participants will also receive a single oral dose of salbutamol twice daily, approximately 15 minutes prior to being given GDC-6988 for 7 days (from Day 8 to Day 14).

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
GDC-6988, salbutamol (albuterol)

Primary outcome(s)
1. Incidence and severity of adverse events, with severity determined according to the Division of AIDS (DAIDS) toxicity grading scale assessed throughout the trial from screening until discharge from the study (approximately 10 weeks)
2. Incidence and severity of vital sign, laboratory test, spirometry, oscillometry, and ECG abnormalities assessed throughout the trial from screening until discharge from the study

(approximately 10 weeks)
3. Incidence and severity of spirometry and oscillometry abnormalities after salbutamol (albuterol) pretreatment assessed throughout the trial from screening until discharge from the study (approximately 10 weeks)

Key secondary outcome(s)
1. Plasma concentration of GDC-6988 and relevant pharmacokinetic (PK) parameters measured from the first dose of GDC-6988 until discharge from the study (approximately 6 weeks)
2. Relationship between GDC-6988 exposure and safety endpoints assessed throughout the trial from the first dose of GDC-6988 until discharge from the study (approximately 6 weeks)

Completion date
02/05/2023

Eligibility

Key inclusion criteria
1. Signed Informed Consent Form
2. Age 18-55 years at time of signing Informed Consent Form
3. Ability to comply with the study protocol
4. Body mass index of 18-32 kg/m² at screening
5. Body temperature of 35-37.5 degrees C at screening and at Day -1
6. Systolic blood pressure of 90 - 150 mmHg and diastolic blood pressure of 50-95 mmHg at screening and at Day -1. Blood pressure should be measured while the subject is in a seated position
7. Agreement to abstain from consumption of caffeine-containing foods and beverages from 72 hours prior to clinic check-in and during the residential stay at the clinic
8. Agreement to abstain from consumption of alcohol from 24 hours prior to clinic check-in and during the residential stay at the clinic
9. FEV1 >80% of predicted at screening and at Day -1
10. Forced vital capacity (FVC) >2.0L by spirometry at screening
11. Ability to demonstrate correct use of the Smart DPI (with placebo capsules) at Screening
12. For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraception, as defined below:
12.1. Women must remain abstinent or use contraceptive methods with a failure rate of <1% per year during treatment and for 28 days after the final dose of study drug
12.2. A woman is considered to be of childbearing potential if she is postmenarchal, has not reached a postmenopausal state (≥12 continuous months of amenorrhea with no identified cause other than menopause), and is not permanently infertile due to surgery (i.e., removal of ovaries, fallopian tubes, and/or uterus) or another cause as determined by the investigator (e.g., Müllerian agenesis). Per this definition, a woman with a tubal ligation is considered to be of childbearing potential. The definition of childbearing potential may be adapted for alignment with local guidelines or regulations.
12.3. Examples of contraceptive methods with a failure rate of <1% per year include bilateral tubal ligation, male sterilization, hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices
12.4. Hormonal contraceptive methods must be supplemented by a barrier method
12.5. The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject
12.6. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not adequate methods of contraception

12.7. If required per local guidelines or regulations, locally recognized adequate methods of contraception and information about the reliability of abstinence will be described in the local Informed Consent Form
12.8. For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agreement to refrain from donating sperm, as defined below:
12.9. With a female partner of childbearing potential or pregnant female partner, men must remain abstinent or use a condom during treatment and for 28 days after final dose of study drug to avoid exposing the embryo. Men must refrain from donating sperm during this same period
12.10. The reliability of sexual abstinence should be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject. Periodic abstinence (e.g., calendar, ovulation, symptothermal, or postovulation methods) and withdrawal are not adequate methods of preventing drug exposure. If required per local guidelines or regulations, information about the reliability of abstinence will be described in the local Informed Consent Form

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
41

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. Women of childbearing potential must have a negative serum pregnancy test result at screening and a negative urine pregnancy test result on Day -1.
2. Study site employee or immediate family member of a study site or Sponsor employee
3. 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
4. Treatment with any immunosuppressive medication within 28 days or 5 drug elimination half-lives, whichever is longer, prior to initiation of study drug
5. Treatment with an herbal or homeopathic remedy within 14 days or 5 drug elimination half-lives (whichever is longer) prior to initiation of study drug
6. 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)
7. Treatment with any other (not already described above) prescription or non-prescription

medication or dietary supplement (products taken by mouth that contain dietary ingredients such as vitamins, minerals, amino acids, herbs or botanicals) within 14 days or 5 drug elimination half-lives, whichever is longer, prior to initiation of study drug, with the following exceptions:
7.1. Oral contraceptives and hormone-releasing intrauterine devices and hormone-replacement therapies
7.2. Acetaminophen or paracetamol at a dose of up to 2 g/day
8. Positive for TB during screening or within 3 months prior to screening, defined as a positive QuantiFERON®-TB Gold test (QFT)
9. Positive HIV test at screening
10. Positive hepatitis B surface antigen (HBsAg) test at screening
11. Positive hepatitis C virus (HCV) antibody test at screening, except in subjects who meet either of the following sets of criteria:
11.1. Subject has undetectable HCV RNA levels for 6 months after completion of HCV anti-viral treatment and a negative HCV RNA test at screening.
11.2. Subject has two negative HCV RNA tests taken at least 7 days apart during screening.
12. Substance abuse, in the investigator's judgment, within 12 months prior to screening, positive urine drug test at screening or Day -1, or positive breath alcohol test at screening or Day -1
13. Positive urine cotinine test at screening or Day -1
14. Use of illicit drugs or hallucinogenic substances (including marijuana) within 28 days prior to screening or on at least 30 days within 2 years prior to screening, or unwillingness to abstain from their use during the study
15. Use of tobacco or nicotine products within 28 days prior to screening or on at least 30 days within 2 years prior to screening, or unwillingness to abstain from their use during the study
16. Receipt of blood products within 120 days prior to screening
17. Hospitalization within 28 days prior to initiation of study drug
18. Anticipation of need for a surgical procedure during the study
19. Infection requiring oral or IV antibiotics within 28 days prior to screening or any evidence of current infection (e.g., bacterial, viral, fungal)
20. In the setting of a pandemic or epidemic, screening for active infections should be considered according to local or institutional guidelines or guidelines of applicable professional societies.
21. Upper or lower respiratory tract infection within 2 weeks prior to initiation of study drug
22. Documented physician-diagnosed asthma for at least 12 months prior to screening
23. Post-bronchodilator reversibility of FEV1 (liters) ≥12% and ≥200 mL at screening
24. Any medical condition or abnormal clinical laboratory finding that, in the investigator's judgment, would preclude the subject's safe participation in and completion of the study or could affect the interpretation of the results Protocol-specified laboratory values must be within the normal reference range for the test laboratory at screening and at Day -1. However, abnormal laboratory values that are not considered to be clinically significant, as determined by the investigator (in consultation with the Medical Monitor, if needed), are permitted.
25. 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
26. History of any significant drug or food allergy (e.g., allergic reactions that resulted in anaphylaxis or hepatotoxicity)
27. History of symptomatic bradycardia
28. History of ataxia or condition associated with ataxia

Please see the clinical protocol for a full list of exclusion criterion, as the list exceeds 5000 characters.

Date of first enrolment

16/08/2022

Date of final enrolment
23/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Quotient Sciences Limited
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Sponsor information

Organisation
F. Hoffman-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

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		29/11/2025	06/01/2026	Yes	No