ISRCTN60385283 https://doi.org/10.1186/ISRCTN60385283

A study to investigate the safety, tolerability, and potential effect of RXC007 in patients with idiopathic pulmonary fibrosis

Submission date 23/04/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 04/05/2022	**Overall study status** Completed	
Last Edited 10/05/2024	**Condition category** Respiratory	

Plain English summary of protocol

Background and study aims
The aim of this study is to investigate the study drug RXC007. The main objectives of this study are as follows:
1. To determine the safety and tolerability (the degree to which side effects of a drug can be tolerated) of RXC007 when it is administered as twice-daily doses over a period of up to 12 weeks (84 days).
2. To investigate the levels of RXC007 in the blood, how this changes over a period of time and to evaluate whether there are differences in the levels between different dose strengths of RXC007.
3. To investigate the effect of RXC007 on the body (known as pharmacodynamics) by analysing the levels of certain biomarkers in the body and to assess the effect of RXC007 on markers associated with idiopathic pulmonary fibrosis (IPF).

Who can participate?
A total of up to 64 patients aged between 40 and 80 years of age with idiopathic pulmonary fibrosis (IPF).

What does the study involve?
This study will comprise three main study groups and two additional sub-study groups. The main study will consist of three planned groups of 16 patients with IPF: each group investigating a different dose strength of RXC007 starting at the lowest planned dose in Group 1 to the highest planned dose in Group 3. The sub-study will consist of two groups of up to 8 patients with IPF (each group respectively evaluating the same dose of RXC007 as evaluated in Group 1 and 3 of the main study). The sub-study groups will include evaluations of the levels of RXC007 found in fluid collected from the lungs.

What are the possible benefits and risks of participating?
It is not known for certain that patients will have any clinical benefit by taking part in the trial although, it is intended that the treatment may provide some benefit. However, this cannot be guaranteed. The information from this study may help to treat future patients with IPF.

Possible risks include the following:
The purpose of the data generated in this study is to provide further information and guidance to support the study sponsor in the development of the study drug RXC007 and to provide early data as to the potential effectiveness of RXC007 as a treatment for IPF.

Blood Sampling:
The procedure for blood collection either by direct venepuncture or indwelling cannula may cause mild pain and bruising at the collection site. The placement of an indwelling catheter is proposed in order to minimise these effects for rapid PK sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time.

Blood Pressure & Heart Rate:
The patients' blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated. Small sticky pads will be placed on the patients' upper body before the ECG. Before the pads are applied, the skin needs to be cleaned. Like Elastoplast®, these sticky pads may be uncomfortable to remove.

COVID-19 Risks:
Patients should also be aware of the risks of exposure to COVID-19. Patients will be required to follow any COVID restrictions and requirements that may be in effect nationally, regionally or in the respective hospital sites. This may include the wearing of masks and COVID-19 testing. Patients will be required to follow all current applicable self-isolation guidelines in the event of a positive COVID-19 test, which may impact their eligibility to continue in the study.

Contraception:
For women of childbearing potential, any patient who is pregnant, breastfeeding or intending to become pregnant will not be eligible for participation. For women of childbearing potential, patients must agree to use two highly effective forms of contraception with their partner using a condom (if applicable) during the study and for at least 3 months following the last dose of study medication.

For males with partners of childbearing potential, patients must not father a child during this study or for a safety period of 3 months following the last dose of study medication. Patients must agree to use two highly effective forms of contraception with their partner using a condom (if applicable) during the study and for at least 3 months following the last dose of study medication. Males who have been sterilised or engage in non-vaginal intercourse should use a condom to prevent exposure of semen to any partner (male or female) until 3 months following the last dose of study medication. Patients must not donate sperm until 3 months following the last dose of study medication.

Spirometry & DLCO:
Performing the lung function and breathing tests may cause some coughing, shortness of breath and lightheadedness. As part of the lung function testing, patients will be required to undergo a lung diffusion test which will measure how well their lungs allow oxygen and carbon dioxide to pass in and out of the blood. For this test, patients may be required to sit in a small chamber known as a body box.
This is a small, confined space (roughly the same size as a standard toilet cubicle) and therefore,

patients may feel claustrophobic during the conduct of this test. The test may take up to 30-45 minutes to complete and patients should notify the staff at any time if they start to feel claustrophobic and the test may be stopped.

CT Scan:
Patients will have a CT scan of the chest on a minimum of 4 occasions (2 scans per timepoint). These procedures use ionising radiation to form images of your body and provide your doctor with other clinical information. The level of radiation exposure per scan is approximately 9.7 milli-Sieverts (mSv) which is a measure of radiation dose). In comparison, a skull X-ray is 0.07 mSv, a chest X-ray is 0.014 mSv and a transatlantic flight is equivalent to 0.08 mSv. The UK average annual dose of ionising radiation exposure from all sources (i.e., natural and man-made) is 2.7 mSv (which goes up to 7.4 mSv for people living in Cornwall). Therefore, the exposure in this study is equivalent to around 2.5 years of background radiation per scan. The risks associated with this have been thoroughly assessed by medical radiation experts and it has been determined that the radiation exposure in this study poses minimal risk.

Bronchoscopy:
As part of the sub-study, participants will be required to undergo a bronchoscopy on two occasions. The procedure itself may cause some discomfort as the bronchoscope is passed through into the lungs but this should resolve once the scope is fully in place. The procedure may take up to 45 minutes to complete. Following the procedure, patients may experience a cough, sore throat, voice loss, and/or fever. The bronchoalveolar lavage procedure will be carried out under full medical supervision and every effort will be made to minimise any imposed risk to patients.

Where is the study run from?
The study will be conducted at several hospital sites across the United Kingdom and Europe.

When is the study starting and how long is it expected to run for?
December 2021 to November 2024

Who is funding the study?
This study is funded and sponsored by a pharmaceutical company called Redx Pharma Plc, based and headquartered in the United Kingdom (UK)

Who is the main contact?
Dr Helen Timmis, Senior Medical Director, Redx Pharma Plc

Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2022-000498-15

Integrated Research Application System (IRAS)
1005138

Protocol serial number
RXC007/0002, IRAS 1005138, CPMS 51888

Study information

Scientific Title
A multi-cohort, randomised, placebo-controlled Phase IIa study to assess the safety, pharmacokinetics, pharmacodynamics and clinical activity of ascending doses of RXC007 in patients with idiopathic pulmonary fibrosis

Acronym
RXC007/0002

Study objectives
The primary objective of the study is:
1. To assess the safety and tolerability of RXC007 when given for 12 weeks (84 days), alone and in combination with nintedanib or pirfenidone

The secondary objectives of the study are:
1. To assess the pharmacokinetic (PK) profile of:
1.1. RXC007, alone and in combination with nintedanib or pirfenidone.
1.2. Nintedanib and pirfenidone at baseline and at steady state in combination with RXC007.
2. To assess the potential of RXC007 to demonstrate clinical activity in patients with idiopathic pulmonary fibrosis (IPF)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 14/06/2022, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; Wales.REC2@wales.nhs.uk), ref: 22/WA/0122

Study design
Open randomized placebo-controlled double-blind trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Idiopathic pulmonary fibrosis (IPF)

Interventions

Approximately 48 patients will be enrolled in three sequential cohorts in the main study and 16 evaluable patients will be enrolled in two sequential cohorts in a parallel translational science sub-study.

The study cohorts will comprise the following:
Main Study Cohorts
Cohort 1
Dose Level 1: 20 mg twice daily
Randomised, double-blind, placebo-controlled
12 weeks (84 days) dosing, comprised of 3 cycles of 28 days, with a safety review by the Dose Review Committee (DRC) when the first 8 patients in Cohort 1 have had 28 days of study treatment.

16 patients, comprising 12 patients randomised to receive RXC007 and 4 patients randomised to receive placebo, to include:
1. At least 4 patients who are not on any IPF treatment
2. At least 4 patients who are receiving nintedanib
3. At least 4 patients who are receiving pirfenidone

Cohort 2
Dose Level 2: 50 mg twice daily
Randomised, double-blind, placebo-controlled
12 weeks (84 days) dosing, comprised of 3 cycles of 28 days*
Cohort 2 may open when 16 patients have been randomised and 8 evaluable patients have completed a minimum of 28 days' dosing in Cohort 1, including a minimum of 4 patients on no background IPF therapy and following a safety review by the DRC.

16 patients, comprising 12 patients randomised to receive RXC007 and 4 patients randomised to receive placebo, to include:
1. At least 4 patients who are not on any IPF treatment
2. At least 4 patients who are receiving nintedanib
3. At least 4 patients who are receiving pirfenidone

Cohort 3
Dose Level 3: 70 mg twice daily
Randomised, double-blind, placebo-controlled
12 weeks (84 days) dosing, comprised of 3 cycles of 28 days
Cohort 3 will open when 16 patients have been randomised and 8 evaluable patients have completed a minimum of 28 days dosing in Cohort 2 and following a safety review by the DRC.

16 patients, comprising 12 patients randomised to receive RXC007 and 4 patients randomised to receive placebo, to include:
1. At least 4 patients who are not on any IPF treatment
2. At least 4 patients who are receiving nintedanib
3. At least 4 patients who are receiving pirfenidone

BAL-Fluid Translational Science Sub Study Cohorts

Cohort 1B
Dose Level 1: 20 mg twice daily
28 days dosing with an option to continue for 84 days

Cohort 3B
Dose Level 3: 70 mg twice daily
28 days dosing with an option to continue for 84 days*
The dose will be the same as Cohort 3 in the main study and may open when the corresponding main study cohort opens.

4-8 patients, comprising 3-6 patients randomised to receive RXC007 and 1 2 patients randomised to receive placebo, all of whom are on no treatment for IPF.
Cohort 1B data will be reviewed after 4 patients and if no biomarker changes are demonstrated, no additional patients will be enrolled at this dose level and the next 4 patients may be assigned to the Cohort 2 dose, once Cohort 2 is open.

*At 12 weeks, at the investigator's discretion and following discussion with the sponsor, patients may be offered RXC0007 treatment beyond Day 84, up to a maximum of 12 weeks after Day 84. Before continuing dosing, patients should discuss any potential alternative treatments with the trial investigator and sign an informed consent form.

The study will consist of the following study visits:

Screening period: Day (D) -28 to D -1

Treatment period:
Cycle (C)1D1 (no time window)
C1D8 (±3 days)
C1D15 (±3 days)
C1D22 (±3 days)
C2D1 (±3 days)
C2D15 (±3 days)
C3D1 (±3 days)
C3D15 (±3 days)
C3D28 - End of Treatment (EOT) (±3 days)

Post-treatment period:
Follow-up (FU)/End of Study (EOS): 30 days after the last dose (-3 days to +7 days)
Overall study duration (for each patient): an approximate study duration of 142 days
The study end is defined as last subject last visit.
The study will take place across several sites within the UK, EU and USA.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
RXC007

Primary outcome(s)
1. The incidence and severity of AEs and serious adverse events (SAEs) recorded from the time of signature of informed consent until 30 days after the last of RXC007/placebo
2. Changes in safety laboratory parameters, vital signs, and ECGs:

2.1. Laboratory safety testing:
Main Study: Screening, Cycle 1: Days 1, 8, 15, 22, Cycles 2 & 3: Days 1, 15 & 28 (Cycle 3 only) & Follow Up
Extended: Cycles 1-3: Day 1 & 15
2.2. Vital signs (blood pressure, heart rate, respiration rate and oral temperature) will be measured at the following timepoints:
Main Study: Screening, Cycle 1: Days 1, 8, 15, 22, Cycles 2 & 3: Days 1, 15 & 28 (Cycle 3 only) & Follow Up
Extended: Cycles 1-3: Day 1 & 15
2.3. ECG (in triplicate): 12-lead ECGs will be measured in triplicate at the following timepoints:
Main Study: Screening, Cycle 1: Days 1, 8, 15, 22, Cycles 2 & 3: Day 1, Day 28 (Cycle 3 only) & Follow Up
Extended: Cycles 1-3: Day 1

All timepoints for assessments are pre-dose timepoints (relative to the morning dose of RXC007)

Key secondary outcome(s))
1. Derived PK parameters calculated from measurement of plasma concentrations of RXC007, nintedanib and pirfenidone: maximum plasma concentration (Cmax) after Dose 1, Cmax at steady state, minimum observed plasma concentration (Cmin) at steady state as well as other relevant parameters (e.g., tmax, t½, λz, AUC0-∞, CL/F, Vz/F, Css, AUCss). Plasma samples for measurement of concentrations as described above will be obtained at the following timepoints:
Main Study Dosing Cycle 1: Days 1 & 8 (pre-dose, 1, 2, 3, 4, 8 h post-dose), Dosing Cycle 2: Day 1
Extended Dosing: Cycles 1-3: Day 1
2. Efficacy parameters derived from measured outcomes of lung function testing (spirometry and carbon monoxide diffusion capacity (DLCO):
2.1. % predicted and absolute volume change from baseline in FVC at 12 weeks (central review)
2.2. % predicted and absolute change from baseline in DLCO at 12 weeks

Assessment of lung function using spirometry will be conducted at the following timepoints:
Main Study Dosing Cycle 1: Days 1, 8, 15, 22 (pre-dose relative to morning dose of RXC007)
Main Study Dosing Cycle 2: Days 1 & 15 (pre-dose relative to morning dose of RXC007)
Main Study Dosing Cycle 3: Days 1, 15 & 28 (pre-dose relative to morning dose of RXC007)
Extended: Cycles 1-3: Days 1 & 15 (pre-dose relative to morning dose of RXC007)

Assessment of lung function using DLCO will be conducted at the following timepoints::
Dosing Cycle 1: Days 1 & 15 (pre-dose relative to morning dose of RXC007)
Dosing Cycle 2: Day 1 (pre-dose relative to morning dose of RXC007)
Dosing Cycle 3: Day 28 (pre-dose relative to morning dose of RXC007)
Extended: Cycles 1-3: Day 1 (pre-dose relative to morning dose of RXC007)

Completion date
06/11/2024

Eligibility

Key inclusion criteria
1. Ability to provide signed and dated informed consent
2. Aged ≥40 to 80 years at the time of signing the informed consent
3. Diagnosis of IPF within 5 years of Screening based on the modified IPF guidelines for diagnosis and management of IPF and confirmed on independent central imaging review

4. Combination of HRCT pattern, as assessed by central reviewers, consistent with diagnosis of IPF
5. FVC % predicted ≥50% predicted of normal at Screening, with no clinically significant deterioration between the Screening Visit and randomisation, as determined by the Investigator
6. DLco (Hb-adjusted) at screening ≥30%
7. In the main study, participants receiving treatment for IPF with nintedanib or pirfenidone are allowed if on treatment for at least 3 months and on a stable dose for at least 4 weeks prior to Screening and during Screening
8. In patients who are not on any treatment for IPF but have previously received nintedanib or pirfenidone, there needs to be a washout period ≥4 weeks prior to Screening
9. No clinically significant history of previous allergy/ sensitivity to RXC007 or any of the excipients contained within the Investigational Medicinal Product (IMP)
10. Blood cell parameters within the following limits:
10.1. Haemoglobin >10 g/dL
10.2. WBC count >3.00 × 10^3/μL
10.3. Neutrophils >1.50 × 10^3/μL
10.4. Platelets >80 × 10^3/μL
11. Alanine transaminase (ALT) and aspartate transaminase (AST) <2x upper limit of normal (ULN). Total bilirubin <1.5 ULN.
12. Negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HbsAg) and hepatitis C virus antibody (HCV Ab) test results at Screening.
13. No clinically significant abnormalities in 12-lead ECG determined within 28 days before first dose of IMP including a QTcF interval >470 ms.
14. No clinically significant abnormalities, in the opinion of the investigator, in vital signs (e.g., blood pressure, pulse rate, respiration rate, oral temperature) within 28 days before first dose of IMP.
15. Patients must be willing to comply with institutional COVID-19 testing policy.
16. Female patients must be surgically sterile, post-menopausal (minimum 1 year without menses), or agree to use two or more of the following forms of highly effective contraception with all male sexual partners from the time of signing the Patient Informed Consent Document (PICD) until 3 months after the last dose of study medication: hormonal (i.e., oral, transdermal, implant, or injection); intrauterine device (IUD), Intrauterine system (IUS) (e.g., Mirena), or bilateral tubal occlusion; vasectomised partner (with appropriate post-vasectomy documentation of the absence of sperm in the ejaculate); or abstinence.
17. Men must use a condom (with spermicide) during the study, and for 3 months after the last dose of study drug, with all sexual partners. Men must not donate sperm for 3 months after the last dose of study drug.

Additional Inclusion Criteria for the Translational Science Sub Study only:
18. Patients must be considered fit to undergo two bronchoscopies, in the opinion of the Investigator.

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
40 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
1. Currently receiving or planning to initiate treatment for IPF with agents not approved for that indication
2. FEV1/FVC ratio <0.7 at Screening, pre-bronchodilator use
3. Lower respiratory tract infection requiring antibiotics within 4 weeks of Screening or during Screening
4. The extent of emphysema in the lungs exceeds fibrosis, based on central review of HRCT scans
5. Need for continuous oxygen supplementation, defined as >15 hours/day
6. Acute IPF exacerbation within 6 months of Screening or during Screening
7. History of ongoing malignant disease, including solid tumours and hematologic malignancies, with the exception of basal cell carcinoma, squamous-cell carcinoma, and carcinoma in situ of the cervix that have been completely excised and considered cured >2 years prior to Screening
8. Significant cardiac disease (e.g., New York Heart Association Class 3 or 4; myocardial infarction within the past 6 months; unstable angina; coronary angioplasty or coronary artery bypass graft within the past 6 months; uncontrolled atrial or ventricular cardiac arrhythmias; or pulmonary hypertension requiring pharmacologic treatment)
9. Clinical diagnosis of any connective-tissue disease (including, but not limited to, scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, and rheumatoid arthritis) or a diagnosis of interstitial pneumonia with autoimmune features as determined by the Investigator applying the recent ERS/ATS research statement. Note: Serological testing is not needed if not clinically indicated
10. Creatinine clearance <60 mL/min according to Cockcroft Gault equation
11. A clinically significant history of GI disorder likely to influence IMP absorption
12. A clinically significant history of infection in the last 3 months
13. Evidence of renal, hepatic, central nervous system, respiratory, cardiovascular, or metabolic dysfunction
14. A clinically significant history of drug or alcohol abuse within the past 3 months prior to Screening
15. Disease other than IPF with a life expectancy of less than 12 weeks
16. Inability to communicate well with the Investigators (i.e., language problem, poor mental development, or impaired cerebral function)
17. Participation in a New chemical entity (NCE) clinical study within the previous 3 months or five half-lives, whichever is longer, or a marketed drug clinical study within the 30 days or five half-lives, whichever is longer
18. Female who is pregnant or breastfeeding
19. Patients who are currently receiving prohibited medications and are unable to stop
20. Patients who are currently receiving steroids or formal anticoagulants (antiplatelet agents are permitted) and are unable to stop
21. Participants who have received a COVID-19 vaccine injection within 72 hours prior to the first dose of IMP

Additional exclusion criteria for the Translational Science Sub Study:
22. Participants with any contra-indication to bronchoscopy and alveolar lavage including tracheal stenosis, pulmonary hypertension, severe hypoxia, or hypercapnia
23. Patients in the sub study are not permitted to receive nintedanib or pirfenidone within 3 weeks of randomisation and throughout the Treatment period

Date of first enrolment
29/06/2022

Date of final enrolment
29/06/2024

Locations

Countries of recruitment
United Kingdom

England

Belgium

Czech Republic

France

Germany

Italy

United States of America

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Royal Brompton Hospital
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Study participating centre
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Sponsor information

Organisation
Redx Pharma (United Kingdom)

ROR
https://ror.org/04wysdg63

Funder(s)

Funder type
Industry

Funder Name
Redx Pharma PLC

Results and Publications

Individual participant data (IPD) sharing plan
The study data will be shared with relevant research groups and external stakeholders collaborating with the study sponsor to support the future development of the IMP within the boundaries of strict confidentiality agreements.

The data-sharing plans for the current study are unknown and will be made available at a later date.

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?
HRA research summary			28/06/2023	No	No