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Phase III study of daraxonrasib (RMC-6236) in previously treated NSCLC patients with RAS mutations

Submission date
09/05/2025

Recruitment status
Recruiting

Registration date
31/10/2025

Overall study status
Ongoing

Last Edited
05/11/2025

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
The aim of this study is to compare the effects of daraxonrasib versus docetaxel in patients with previously treated locally advanced or metastatic non-small cell lung cancer (NSCLC) with a mutation in the RAS oncogene.

Who can participate?
Patients aged 18 years and over with NSCLC with a RAS mutation

What does the study involve?
There will be a pre-screening period up to 14 days during which study doctors will see if the patient's tumor has a RAS mutation. This is followed by a screening period up to 28 days (when patients meet with study doctors and undergo tests to see if they can join the study). This is followed by a treatment period and a follow-up period. During the treatment period, half of the patients will receive daraxonrasib and the other half will receive docetaxel. This is followed by a treatment period and a follow-up period.

What are the possible benefits and risks of participating?
Docetaxel is an approved drug commonly used to treat patients with NSCLC and the side effects are well-known. Daraxonrasib is currently being investigated in ongoing clinical studies; therefore, all the possible side effects are not fully known at this time. As with any drug, an allergic reaction can occur after taking or receiving any study treatment. Allergic reactions can be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or breathing difficulties. Daraxonrasib may have some or all of the side effects listed in this section. It is also possible that they might have other side effects that are not listed in the table below. As with any experimental drug, unknown and potentially serious or life-threatening side effects could occur from the study treatment you may receive during the study. Once the study drug(s) is/are stopped, it is not known how long the side effects will last.
The following are the most common side effects (may affect more than 1 in 10 people) that have been reported in the clinical trial for patients taking daraxonrasib monotherapy (daraxonrasib

alone): rash, nausea/vomiting, fatigue (feeling tired)/loss of energy or strength, diarrhoea, constipation, scaliness or thickening of the skin, painful inflammation and/or sores in the mouth and gums, effects on the kidneys and urinary tract, including protein in the urine or changes in the salts in the blood, inflammation of the liver and/or abnormal blood tests, and decrease in red blood cells (cells that carry energy and oxygen in the blood).
The most common side effects reported with docetaxel are: infections, decrease in white blood cells (with or without fever), decrease in red blood cells, exaggerated response by the immune system to the drug, low number of platelets (which may cause bleeding and bruising), damage to the nerves (which can cause numbness, pain, and weakness), taste disorder, shortness of breath, constipation, loss of appetite, nail disorders, fluid retention, feeling weak, joint and muscle pain, nausea, diarrhoea, vomiting, mouth sores, hair loss, skin reactions, and muscle aches.
The following serious and/or severe side effects have been reported with docetaxel: second cancer, skin reactions (redness of hands and feet with swelling followed by peeling), nervous system reactions (tingling/numbness, intense sensation, and pain), eye disorders (retina swelling), feeling weak, unborn baby toxicity, and tumour lysis syndrome (breakdown/death of tumour cells releases cell contents into the blood, causing damage to organs).
Allergic reactions to the radioactive tracer are rare but could occur. Occasionally, some soreness or swelling may develop at the injection site. These symptoms can usually be relieved by applying moist, warm compresses to your arm. There is always a slight risk of damage to cells or tissue from being exposed to any radiation, including the low level of radiation released by the radioactive tracer used for this test.
As part of the CT scans, you will be given a radioactive contrast dye by mouth and/or by an injection through your vein, which will expose you to a small amount of radiation. A person who has allergies is more likely to have an allergic reaction to the dye. This reaction may be mild, such as a skin rash or hives, or severe, such as breathing difficulties or shock.
An MRI scan uses radio waves and a strong magnetic field to provide images of internal organs and tissues. Because an MRI scanner uses strong magnets, you cannot have any metal implants in your body when you have an MRI
They may feel some amount of pain or discomfort during the biopsy, including pain when a local anesthetic is injected by needle to numb the area, pressure and pain where the biopsy needle is inserted, discomfort from lying still for a long time, and soreness at the biopsy site. Although not common, there is a risk of abnormal wound healing, bleeding, damage to nearby tissues or organs, fever, infection, and allergic reaction to the anesthetic.
Taking blood from a vein (usually in the arm) may cause local pain, bruising, occasional light-headedness, fainting, and very rarely, infection at the site of the blood draw. A small hollow plastic catheter may be placed in the vein on days when for blood sample collection on days when frequent sampling is required.

Where is the study run from?
Revolution Medicines (USA)

When is the study starting and how long is it expected to run for?
May 2025 to December 2030

Who is funding the study?
Revolution Medicines (USA)

Who is the main contact?
Revolution Medicines Study Director, medinfo@revmed.com

Plain English summary under review with external organisation

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1011716

ClinicalTrials.gov (NCT)
NCT06881784

Protocol serial number
RMC-6236-301

Study information

Scientific Title

RASolve 301: Phase III multicenter, open-label, randomized study of daraxonrasib versus docetaxel in patients with previously treated locally advanced or metastatic RAS[MUT] NSCLC

Acronym
RASolve 301

Study objectives
To compare the treatment effect of daraxonrasib versus docetaxel in the RAS (G12X-C) population.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 24/06/2025, North of Scotland Research Ethics Committee (Summerfield House, 2 Eday Road, Aberdeen, AB15 6RE, UK; +44 (0)1224558458; gram.nosres@nhs.scot), ref: 25/NS/0056

Study design
Randomized controlled open-label parallel-group study

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
RAS mutant non-small cell lung cancer

Interventions
Experimental:daraxonrasib oral tablets
Active comparator:docetaxel intravenous (IV) infusion as the standard of care therapy

Frequency: once daily
Route of administration: oral
Duration of treatment: up to 4 years
Randomization process: via Interactive Response Technology system

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Docetaxel, daraxonrasib (RMC-6236)

Primary outcome(s)
In the RAS (G12X-C) population, i.e., RAS G12X excluding G12C, the treatment effect of daraxonrasib versus docetaxel on:

1. Progression-free survival (PFS) (per Investigator) evaluated at disease progression or death from any cause, whichever occurs first. Progression is per RECIST v1.1 as assessed by the Investigator
2. Overall survival (OS), evaluated at death from any cause

Key secondary outcome(s))
1. In the RAS (MUT) population, the treatment effect of daraxonrasib versus docetaxel on:
1.1. PFS (per Investigator) evaluated at disease progression or death from any cause, whichever occurs first. Progression is per RECIST v1.1 as assessed by the Investigator
1.2. OS, evaluated at death from any cause
2. In the RAS (G12X-C) and RAS (MUT) populations, the treatment effect of daraxonrasib versus docetaxel on objective response (per Investigator) of partial response (PR) or complete response (CR) per RECIST v1.1 as assessed by the Investigator. Responses require confirmatory repeat radiologic assessment at no less than 4 weeks after the original response.

Completion date
01/12/2030

Eligibility

Key inclusion criteria
1. At least 18 years of age and has provided informed consent
2. ECOG performance status 0 or 1
3. Histologically confirmed NSCLC, either locally advanced or metastatic, not amenable to curative surgery or radiotherapy
4. Measurable disease per RECIST v1.1
5. Adequate organ function (bone marrow, liver, kidney, coagulation)
6. One to two prior lines of therapy, including an anti-PD-1/anti-PD(L)-1 agent and platinum-based chemotherapy
7. Documented RAS mutation status, defined as nonsynonymous mutations in KRAS, NRAS, or HRAS at codons 12, 13, or 61(G12, G13, or Q61)
8. Able to take oral medications

For the full list of inclusion criteria, please refer to the protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Prior therapy with any direct RAS-targeted therapy or docetaxel
2. Untreated central nervous system (CNS) metastases
3. Medically significant comorbidities (significant cardiovascular disease, lung disease, or impaired GI function)
4. Ongoing anticancer therapy
5. Pregnant or breastfeeding
6. Other driver mutations for which an approved targeted therapy is available

For the full list of exclusion criteria, please refer to the protocol

Date of first enrolment
07/05/2025

Date of final enrolment
01/01/2027

Locations

Countries of recruitment
United Kingdom

Australia

Belgium

France

Germany

Hong Kong

Ireland

Italy

Japan

Netherlands

New Zealand

Poland

Puerto Rico

Singapore

Spain

Switzerland

Taiwan

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
Revolution Medicines (United States)

ROR
https://ror.org/00mny1y94

Funder(s)

Funder type
Industry

Funder Name
Revolution Medicines

Alternative Name(s)
Revolution Medicines, Inc., REVOLUTION Medicines Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publicly available repository (pseudonymized data in Medidata Database housed by Aperio, Inc.)

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes