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Phase II study of MRTX849 monotherapy and in combination with pembrolizumab in patients with advanced non-small-cell lung cancer with KRAS G12C mutation

Submission date
24/02/2022

Recruitment status
No longer recruiting

Registration date
03/05/2022

Overall study status
Completed

Last Edited
22/10/2026

Condition category
Cancer

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

Plain English summary of protocol

Background and study aims
The aim of this study is to evaluate the effectiveness of the investigational medication MRTX849, given alone or in combination with the cancer therapy pembrolizumab, in patients with non-small cell lung cancer (NSCLC) who have a specific change in a tumour gene (KRAS G12C mutation). This evaluation will include looking at how effective this treatment is in reducing and controlling the cancer. Other aims of the study include assessing what side effects occur and how often they occur, how quickly MRTX849 is absorbed into the bloodstream, and how fast it is removed by the body. Several laboratory tests will be performed using samples of tumour tissue or blood to understand how and why the combination of medications may work.

Who can participate?
Patients with advanced non-small-cell lung cancer with KRAS G12C mutation

What does the study involve?
Participants will be randomly allocated to one of three treatment groups that will receive either MRTX849 and pembrolizumab or MRTX849 alone. Study treatment will be administered in 21-day cycles until one of the indications for stopping treatment is identified such as disease progression, unacceptable adverse reaction(s) or receipt of the maximum number of cycles per local standard-of-care.

What are the possible benefits and risks of participating?
The potential risks and burdens for this study are provided in the participant information sheet and informed consent forms. The participants will therefore know about these risks and burdens before taking part in the study. Study staff will be trained on the expected side effects associated with the study drugs. They will also be trained on how to report unexpected reactions and given the contact details for the appropriate contact to discuss management and treatment of these side effects. Female participants are advised not to become pregnant during the study or within 6 months of completing treatment. Pregnancy tests will be performed before the

administration of the study drugs. Both male and female participants are advised to use contraception for the duration of participation in the study. Should a partner of a participant become pregnant during this study they will be advised on the risks and will be invited to consent to additional assessment of the mother and child by the study team during and after the pregnancy.

Where is the study run from?
Mirati Therapeutics (USA)

When is the study starting and how long is it expected to run for?
February 2022 to August 2024

Who is funding the study?
Mirati Therapeutics (USA)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT04613596

Clinical Trials Information System (CTIS)
2020-003101-58

Integrated Research Application System (IRAS)
1004279

Central Portfolio Management System (CPMS)
51494

Protocol serial number
849-007

Study information

Scientific Title
A Phase II trial of MRTX849 monotherapy and in combination with pembrolizumab in patients with advanced non-small-cell lung cancer with KRAS G12C mutation

Study objectives
1. To evaluate the efficacy of MRTX849 monotherapy and in combination with pembrolizumab administered in the first-line treatment setting to patients having non-small-cell lung cancer (NSCLC) with KRAS G12C mutation
2. To characterize the safety and tolerability of the monotherapy and the combination regimen in the selected population
3. To evaluate secondary efficacy endpoints using monotherapy and the combination regimen in the selected population
4. To evaluate the pharmacokinetics (PK) of MRTX849 administered as monotherapy and in combination with pembrolizumab

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval pending, REC ref: 22/EE/0062

Primary study design
Interventional

Study design
Randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Advanced non-small cell lung cancer

Interventions

This is a study involving an investigational (experimental) medication called MRTX849, being developed by Mirati Therapeutics, Inc.

In this study, participants will be administered MRTX849 monotherapy (alone) or MRTX849 in combination with pembrolizumab, an immunotherapy that has not yet been approved by the regulatory authorities such as the Medicines & Healthcare products Regulatory Agency (MHRA) in the UK for the treatment of lung cancer in several settings.

The study will include participants with locally advanced or metastatic NSCLC harbouring the KRAS-G12C mutation. Participants will be enrolled and treated in three cohorts (groups) as defined by their tumour proportion score (TPS) determined through assessment of extra signal molecules (PD-L1 molecules) found on the surface of the tumour cells. Up to 250 participants across approximately 110 study sites globally are expected to participate in this study.

Participants in this study will receive treatment based on the results of their PD-L1 testing (a marker that looks at how the immune system is involved in a cancer).

If the PD-L1 result is “negative” (less than (<) 1%), the participants will be randomly assigned to one of two groups through an online tool called IRT, to receive the following treatments listed below:

Cohort 1a: MRTX849 (400 mg dose) twice daily in combination with a standard treatment for lung cancer (pembrolizumab)
OR
Cohort 1b: MRTX849 (600 mg dose) twice daily

If the PD-L1 result is “positive” (1% or (>) greater), the participant will receive the following treatment listed below:

Cohort 2: MRTX849 (400 mg dose) twice daily in combination with (pembrolizumab) which is the standard treatment for lung cancer.

Participants may remain on the study treatment for as long as their disease doesn’t get worse such that the study doctor feels they should stop study treatment, and as long as they tolerate the medication (the side effects are not typically severe), and they wish to continue.

All participants will be followed for adverse events (AEs) for at least 28 days after the last dose of study treatment. All participants will be followed for serious adverse events (SAEs) for 90 days following the last dose of study treatment or, if subsequent therapy is begun, at least 28 days following the last dose of study treatment.

For participants who discontinue study treatment for a reason other than objective disease progression, disease assessment should continue until objective disease progression is documented by the investigator or start of subsequent anti-cancer therapy, whichever is sooner. Survival status and subsequent anti-cancer therapies will be collected during long term follow-up until death or lost to follow-up.

Intervention Type

Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
MRTX849, pembrolizumab

Primary outcome(s)
Objective Response Rate (ORR) assessed using Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 at 22 months

Key secondary outcome(s)
1. Safety characterized by type, incidence, severity, timing, seriousness and relationship to study treatment of adverse events and laboratory abnormalities at 22 months
2. Duration of response (DOR) estimated using the Kaplan-Meier method at 22 months
3. Pharmacokinetics (PK) of MRTX849 administered as monotherapy and in combination with pembrolizumab by measuring blood plasma MRTX849 and potential metabolite concentrations at 22 months

Completion date
31/08/2024

Eligibility

Key inclusion criteria
1. Histologically confirmed diagnosis of NSCLC (squamous or nonsquamous) with KRAS G12C mutation and known PD-L1 Tumor Proportion Score (TPS) score
2. Unresectable or metastatic disease

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Prior systemic treatment for locally advanced or metastatic NSCLC including chemotherapy, immune checkpoint inhibitor therapy, or a therapy targeting KRAS G12C mutation (e.g., AMG 510)
2. Active brain metastases

Date of first enrolment
23/11/2020

Date of final enrolment
31/08/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Australia

Austria

Belgium

Canada

China

Germany

Hungary

Ireland

Israel

Italy

Netherlands

New Zealand

Poland

Portugal

Singapore

Spain

Taiwan

Study participating centre

The Christie
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Study participating centre
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GU2 7XX

Sponsor information

Organisation
Mirati Therapeutics (United States)

ROR
https://ror.org/01by01460

Funder(s)

Funder type
Industry

Funder Name
Mirati Therapeutics

Alternative Name(s)
Mirati Therapeutics Inc, Mirati Therapeutics, 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 and/or analysed during the current study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?

Abstract results	28/05/2025	22/10/2026	No	No
HRA research summary		28/06/2023	No	No