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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
09/11/2022

Condition category
Cancer

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

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

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Scientific

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Additional identifiers

EudraCT/CTIS number
2020-003101-58

IRAS number
1004279

ClinicalTrials.gov number
NCT04613596

Secondary identifying numbers
849-007, IRAS 1004279, CPMS 51494

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

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)

Treatment

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

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

Secondary outcome measures
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

Overall study start date
21/02/2022

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

Age group
Adult

Sex
Both

Target number of participants
250

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
Australia

Austria

Belgium

Canada

China

England

Germany

Hungary

Ireland

Israel

Italy

Netherlands

New Zealand

Poland

Portugal

Scotland

Singapore

Spain

Taiwan

United Kingdom

Study participating centre
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Study participating centre
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Sponsor information

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Sponsor type
Industry

Website
https://www.mirati.com/

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

Publication and dissemination plan
1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Publication on website
5. Other publication
6. Submission to regulatory authorities
7. Fully anonymised and aggregated data will be used. Participants will have the option for their data to be used for future research which will not directly identify the participants. The sponsor may share anonymised data collected during this study with others. The data provided to others will not include information that identifies the participant.

Intention to publish date
31/12/2026

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?
HRA research summary			28/06/2023	No	No