A phase Ib/II open-label, multi-center dose escalation study of JDQ443 in patients with advanced solid tumors harboring the KRAS G12C mutation

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This study has been transitioned to CTIS with ID 2023-508073-87-00 check the CTIS register for the current data. Primary objectives:Dose Escalation• To assess the safety and tolerability of JDQ443 single agent and JDQ443 in combination with TNO155,...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON54361

Source
ToetsingOnline

Brief title
CJDQ443A12101

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Advanced solid tumors harboring KRAS G12C mutation

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Farmaceutische industrie.

Intervention

Keyword: JDQ443, KRASC12C-mutation, TNO155, VDT482

Outcome measures

Primary outcome

For all groups, Best Overall Response (BOR), Overall Response Rate (ORR), Duration of Response (DOR), Disease Control Rate (DCR), Progression Free Survival, (PFS) and Overall Survival (OS) per RECIST 1.1

For the brain metastasis group, Overall Intracranial Response Rate (OIRR), Intracranial Disease Crontrol Rate (IDCR), Best Overall Intracranial Response (BOIR), Duration of Intracranial Response (DOIR), and intracranial progression free survival (IPFS) per mRANO-BM.

Secondary outcome

• Concentration and PK parameters of JDQ443, TNO155, and / or tislelizumab.

• Incidence of antidrug antibodies to tislelizumab

• Incidence and severity of adverse events and serious adverse events, including changes in laboratory values, electrocardiograms, and vital signs.

• Frequency of dose interruptions, reductions, and dose intensity by treatment.

• Incidence and severity of dose limiting toxicities (DLTs)(dose escalation only)

Study description

Background summary

Better treatments are needed for patients harboring the KRAS G12C mutation. JDQ443 is a potent and selective inhibitor of mutant KRAS G12C, which is a common driver of oncogenic signaling in a number of different types of tumors. Targeted inhibition of KRAS G12C via JDQ443 may result in robust antitumor responses.

Study objective

This study has been transitioned to CTIS with ID 2023-508073-87-00 check the CTIS register for the current data.

Primary objectives:
Dose Escalation
• To assess the safety and tolerability of JDQ443 single agent and JDQ443 in combination with TNO155, JDQ443 in combination with tislelizumab, and JDQ443 in combination with TNO155 and tislelizumab, and to identify the maximum tolerated dose and/or recommended dose and regimen for future studies.
Dose Expansion
• To evaluate the overall response rate (ORR) for JDQ443 single agent and JDQ443 in combination with TNO155, JDQ443 in combination with tislelizumab, and JDQ443 in combination with TNO155 and tislelizumab.
• To evaluate the preliminary overall intracranial response rate (OIRR) of JDQ443 single agent (brain metastasis group only)
• To evaluate the preliminary safety/tolerabilityand anti-tumor activity of JDQ443 single agent in patients with NSCLC (JDQ443 dose randomization group only)

Secondary objectives:
To evaluate the anti-tumor activity of the study treatments.
• To further characterize the safety and tolerability of the study treatments (dose expansion part only).
• To characterize the PK of JDQ443 single agent and PK of JDQ443, TNO155, and tislelizumab in JDQ443 in combination with TNO155, JDQ433 in combination with tislelizumab and JDQ443 in combination with TNO155 and tislelizumab
• To evaluate the immunogenicity of tislelizumab when dosed in combination with JDQ443 and / or TNO155.
• To evaluate the intracranial preliminary anti-tumor activity of JDQ443 single agent (brain metastasis group only)

A food effect cohort will be done to examine the influence of medication intake when patient hasn't eaten versus when the patient has had food prior to intake

of medication.

Study design

This is a phase Ib/II open label study. The escalation part will characterize the safety and tolerability of JDQ443 single agent and JDQ443 in combination with the other study treatments (TNO155 and tislelizumab) in advanced solid tumor patients. After the determination of the maximum tolerated dose / recommended dose for a particular treatment arm, dose expansion will assess the anti-tumor activity and further assess the safety, tolerability, and PK/PD of each regimen at the maximum tolerated dose / recommended dose.

Intervention

JDQ443, tislelizumab (VDT482), TNO155

Study burden and risks

Risks and side-effects associated with the treatment provided. Risks associated with the study assessments suchs as blooddraws, imaging and tumor biopsy. Burdens: 3 week cycles, cycle 1: 4 visits, cycle 2 & 3: 3 visits, from C4 onwards 1 visit per cycle. Assessments during visits, depending on mono- or combination therapy and type of visit: physical exam, blooddraws, ECGs / vital signs, imaging, pregnancy testing, tumor biopsy.

Contacts

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Novartis

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Dose Escalation:
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant solid tumors who have received standard of care therapy or are intolerant or ineligible to approved therapies.
Dose Expansion:
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant non-small cell lung cancer who have received a platinumbased chemotherapy regimen and immune checkpoint inhibitor therapy, unless patient was ineligible to receive such therapy. Treatment with a prior KRAS G12C inhibitor is not allowed.
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant non-small cell lung cancer who have received a platinumbased chemotherapy regimen and immune checkpoint inhibitor therapy, unless patient was ineligible to receive such therapy, and one treatment line of a direct KRAS G12C inhibitor given as a single agent and discontinued within 6 months of the first day of study treatment.
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant NSCLC who have received a platinum-based chemotherapy regimen and an immune checkpoint inhibitor therapy either in combination or in sequence, unless patient was ineligible to receive such therapy. The patient must have at least one untreated brain metastasis. Treatment with a prior KRAS G12C inhibitor is not allowed.
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant colorectal cancer who have received standard-of-care therapy, including a fluropyrimidine-, oxaliplatin-, and irinotecanbased chemotherapy, unless patient was ineligible to such therapy. Treatment with a prior KRAS G12C inhibitor is not allowed.
• Patients with advanced (metastatic or unresectable) KRAS G12C mutant solid tumors other than NSCLC or CRC who have received standard of care therapy or are intolerant or ineligible to approved therapies. Treatment with a prior KRAS G12C inhibitor is not allowed.
All Patients:
• ECOG performance status of 0 or 1.

• Patients must have a site of disease amenable to biopsy and be a candidate for tumor biopsy according to the institution*s own guidelines and requirements for such procedures.

Exclusion criteria

Tumors harboring driver mutations that have approved targeted therapies, with the exception of KRAS G12C mutations.
• Prior treatment with a KRAS G12C inhibitor is excluded for patients in the single agent dose escalation arm and a subset of groups in dose expansion.
• Prior treatment with a SHP2 or SOS1 inhibitor is not allowed for NSCLC patients enrolled into the dose expansion parts of the JDQ443 single agent and JDQ443 plus TNO155 expansion arms.
• Untreated brain metastases (applicable to all patients except the brain metastasis group), symptomatic brain metastases (applicable to all patients), or known leptomeningeal disease (applicable to all patients)
• Clinically significant cardiac disease or risk factors at screening
• Insufficient bone marrow, hepatic or renal function at screening

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-07-2021
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	NA
Generic name:	tislelizumab

Ethics review

Approved WMO Date:	01-03-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-04-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-10-2021
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	26-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-01-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-05-2022
Application type:	Amendment

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Approved WMO Date:	20-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	29-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-11-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-02-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-03-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-07-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	08-08-2023
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	27-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-05-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2023-508073-87-00
EudraCT	EUCTR2020-004129-22-NL
ClinicalTrials.gov	NCT04699188
CCMO	NL75349.031.21