An open label, multi-center roll-over study to assess long-term safety in patients who are ongoing or have completed a prior global Novartis or GSK sponsored Tafinlar (dabrafenib) and/or Mekinist (trametinib) study and are judged by the investigator to benefit from continued treatment

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This study has been transitioned to CTIS with ID 2023-509318-13-00 check the CTIS register for the current data. This is an open-label, multi-center, roll-over study designed to provide continued access to subjects who have previously participated…

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

Summary

ID

NL-OMON51217

Source
ToetsingOnline

Brief title
CDRB436X2X02B

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
various rare malignant tumors

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: Dabrafenib, rare tumors, Trametinib

Outcome measures

Primary outcome

The primary objective is to evaluate long term safety as assessed by occurrence

of AEs/SAEs. Endpoint: Frequency and severity of AEs/SAEs

Secondary outcome

To evaluate clinical benefit as assessed by the Investigator. Endpoint:

Proportion of subjects with clinical benefit as assessed by the

Investigator at scheduled visits.

Study description

Background summary

The purpose of this roll-over study is to better characterize long-term safety in patients who are receiving treatment with dabrafenib and/or trametinib in a Novartis-sponsored Global Drug Development (GDD), Global Medical Affairs (GMA) or a former GSK-sponsored study that has reached its study objectives, and are unable to access dabrafenib and/or trametinib outside of a clinical trial.
Subjects must be benefiting from treatment on the parent study as judged by the Investigator.

Study objective

This study has been transitioned to CTIS with ID 2023-509318-13-00 check the CTIS register for the current data.

This is an open-label, multi-center, roll-over study designed to provide continued access to subjects who have previously participated in a dabrafenib and/or trametinib parent study and who have fulfilled the requirements for the primary objective, and who in the opinion of the Investigator, would benefit from continued treatment. At the completion of their parent study, subjects may be eligible to continue into the roll-over study in order to receive treatment for as long as they continue to demonstrate benefit, or until one of the discontinuation criteria is met.

Study design

Subjects will be enrolled from parent studies for the treatment of BRAF V600 mutation positive tumors which may include, but are not limited to, unresectable or metastatic melanoma, NSCLC, ATC, biliary tract cancer, gastrointestinal stromal tumors, high-grade glioma, low-grade glioma,non-seminomatous/non-germinomatous germ cell tumors, adenocarcinoma of small intestine, colorectal cancer, hairy cell leukemia, and multiple myeloma. Subjects in this study may receive one of the following treatments received in the parent study which are:
* Subjects who received monotherapy of either of dabrafenib or trametinib solid dose forms
* Subjects who received combination of dabrafenib and trametinib solid dose forms
There will be no screening period for this study. Once eligible subjects provide consent, they can start treatment with study drug as soon as they enter the study. All subjects must report to the study site for their first visit and commence study participation. Subject should return to the study center for resupply of study medication, clinical and safety assessment every 12 weeks (+/- 2 week). The subject may return to the study site at any given time for routine clinical assessments and local standard of care, however data from these visits, outside from what is specified in this protocol will not be captured in the eCRF. At every quarterly visit, the Investigator is required to confirm that the subject continues to have favorable clinical benefit and may continue receiving study treatment. All adverse events and serious adverse events will be collected continuously throughout the study. Subjects will continue to be treated until one of the discontinuation criteria is met. A subject will reach the end of study when dabrafenib and/or trametinib is permanently discontinued and the end of treatment visit has been performed. All subjects will be followed up for safety for 30 days after the last dose of study or until SAE is resolved as required, whichever is later. The study duration will be assessed 10 years after the first subject*s first visit in this clinical study, or will remain open until treatment becomes commercially available and reimbursed, or another access program becomes available,

whichever comes first.

Intervention

Treatment with dabrafenib and trametinib.

Study burden and risks

Side effects of treatment
Hospital visits: every 12 weeks until progression.
Prenancytest (if relevant) every month at home (urine test).
Prenancytest (if relevant) baseline and end of treatment visit (in clinic, blood).

Contacts

Public
Novartis

Haaksbergweg 16
Amsterdam 1101 BX
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Scientific
Novartis

Haaksbergweg 16
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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Patients eligible for inclusion in this study have to meet all of the following criteria:
1. Patient is currently receiving treatment with dabrafenib and/or trametinib monotherapy or combination within a Novartis or former GSK sponsored study which has fulfilled the requirements for the primary objective.
2. In the opinion of the Investigator would benefit from continued treatment.
3. Patient has demonstrated compliance, as assessed by the Investigator, within the parent study protocol requirement(s).
4. Willingness and ability to comply with scheduled visits, treatment plans and any other study procedures.
5. Written informed consent obtained prior to enrolling in the roll-over study and receiving study medication. If consent cannot be expressed in writing, it must be formally documented and witnessed, ideally via an independent trusted witness.
6. Does not require treatment with prohibited concomitant medications

Exclusion criteria

Subjects eligible for this study must not meet any of the following criteria:
1. Subject has been previously permanently discontinued from study treatment in the parent protocol due to any reason.
2. Subject*s indication is commercially available and reimbursed in the local country.
3. Subject currently has unresolved toxicities for which dabrafenib and/or trametinib dosing has been interrupted in the parent study.
4. Pregnant or nursing (lactating) women who are lactating must discontinue nursing prior to the first dose of study treatment and must refrain from nursing throughout the treatment period and for 4 months following the last dose of study treatment.
5. Women of childbearing potential, defined as all women physiologically capable of becoming pregnant, must use highly effective methods of contraception during dosing and for 16 weeks after stopping treatment with trametinib (for trametinib monotherapy trials); 2 weeks after stopping treatment with dabrafenib (for dabrafenib monotherapy trials); 16 weeks after stopping treatment with trametinib or 2 weeks after stopping treatment with dabrafenib whichever is longer (for trials of dabrafenib in combination with trametinib). For more information, please refer to the protocol.
6. Sexually active males (including those that have had a vasectomy) taking the dabrafenib and/or trametinib therapy must use a condom during intercourse, and should not father a child during this period. The minimum amount of time a subject must use a condom after last treatment is as follows:
• 16 weeks post treatment discontinuation dabrafenib in combination with

trametinib
• 2 weeks after treatment with dabrafenib monotherapy
• 16 weeks after treatment with trametinib monotherapy

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-09-2021
Enrollment:	3
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Mekinist
Generic name:	Trametinib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tafinlar
Generic name:	Dabrafenib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-06-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	07-07-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-12-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-09-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	09-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-07-2023
Application type:	Amendment
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Approved WMO Date:	05-10-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-10-2023
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Approved WMO Date:	05-02-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-03-2024
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2023-509318-13-00
EudraCT	EUCTR2017-001987-39-NL
CCMO	NL76683.041.21