An open label, multi-center roll-over study to assess long-term effect in pediatric patients treated with Tafinlar (dabrafenib) and/or Mekinist (trametinib)

Published: 26-10-2022
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This study has been transitioned to CTIS with ID 2023-509276-42-00 check the CTIS register for the current data. Primary:To assess the long-term safety of treatment with dabrafenib, trametinib or the combination.Secondary:To assess the long-term…

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

Summary

ID

NL-OMON51275

Source
ToetsingOnline

Brief title
CDRB436G2401

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
gliomas; brain tumors

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Dabrafenib, Pediatric, Roll-over, Trametinib

Outcome measures

Primary outcome

Frequency and severity of (serious) adverse events.

Secondary outcome

Efficacy parameters according to the local standards, at least every 6 months.

Study description

Background summary

This is a global single-arm, open-label, multi-center study to collect data on the long-term effects of dabrafenib, trametinib or the combination in pediatric subjects who have been treated on Novartis sponsored trials. No formal hypothesis will be tested. Additionally, this study will provide continued access to study medication(s) for subjects who have previously participated in dabrafenib and/or trametinib treatment studies (parent studies):
CDRB436G2201 (The only study that was performed in the Netherland): Phase II open-label global study to evaluate the effect of dabrafenib in combination with trametinib in children and adolescent patients with BRAF V600-mutation positive Low Grade Glioma (LGG) or relapsed or refractory High Grade Glioma (HGG).
CDRB436A2102: Phase I/IIa, 2-part, multi-center, single-arm, open-label study to determine the safety, tolerability and pharmacokinetics of oral dabrafenib in children and adolescent patients with advanced BRAF V600-mutation positive solid tumors.
CTMT212X2101: Pharmacodynamics and clinical activity of the MEK inhibitor trametinib in children and adolescents patients with cancer or plexiform neurofibromas and trametinib in combination with dabrafenib in children and adolescents with cancers harboring V600 mutation.
The participants were aged between 1 and 17 years of age at the time of enrollment in the parent study.

Dabrafenib (trade name Tafinlar) is a BRAF-inhibitor. It is a targeted cancer inhibiting therapy. Trametinib (trade name Mekinist) is a MEK-inhibitor; a targeted cancer inhibiting therapy as well. The combination of both drugs has been granted marketing authorization in the EU for the treatment of adults with certain melanomas and metastatic non- small cell lung cancer. Treatment of children and adolescents has not received marketing approval yet.
This study is part of the development program of dabrafenib and trametinib for children and adolescents up to and including 17 years of age.

Study objective

This study has been transitioned to CTIS with ID 2023-509276-42-00 check the CTIS register for the current data.

Primary:
To assess the long-term safety of treatment with dabrafenib, trametinib or the combination.
Secondary:
To assess the long-term effect of treatment with dabrafenib, trametinib or the combination on general health, growth and development.
To assess efficacy as determined by institutional standard of care procedures.

Study design

This is a global single-arm, open-label, multi-center study to collect data on the long-term effects of dabrafenib, trametinib or the combination in pediatric subjects who have been treated on Novartis sponsored trials. No formal hypothesis will be tested. Additionally, this study will provide continued access to study medication(s) for subjects who have previously participated in dabrafenib and/or trametinib treatment studies (parent studies).

Intervention

Treatment with the combination of dabrafenib and trametinib, as in the parent study CDRB436G2201, the only parent study that was performed in NL). Subjects are to use the study treatment based on the parent protocol. The starting dose should be the same dosage the subject was receiving at the last visit or at the completion of the parent study.

Study burden and risks

Risk: Adverse events of the study medication.
Burden:
During the treatment period:
• Contact every 3 months. Yearly: month 3 and 9: by phone or in person; month 6 and 12: in the hospital.

• Physical examination month 6, 12. Dermatological examination month 12. Tanner score month 12.
• Blood tests (fasting, approx. 15 mL) month 6, 12.
• Pregnancy test (if relevant) every month (if necessary at home, result to be communicated to investigator by phone).
• Urine test month 12.
• Best corrected visual acuity month 6, 12.
• EKG and echocardiography (or MUGA-scan) month 6, 12.
• X-ray wrist or tibia (for bone age) month 12.
During follow-up period when study treatment has been discontinued and disease has not progressed:
• Hospital visit every 12 weeks.
• Physical examination, including dermatological examination and Tanner score.
• Blood tests.
• EKG.
• Bone age.
Optional during or after the study:
• Use of data and remaining body material for other research.
During follow-up period when study treatment has been discontinued and disease has progressed:
• Every 6 to 12 months phone call.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

Subjects eligible for inclusion in this study must meet all of the following criteria:
All subjects
1. Written informed consent, according to local guidelines, signed by the patients and / or by the parents or legal guardian prior to any study related screening procedures are performed.
2. Participation in a Novartis sponsored study such as TMT212X2101, DRB436G2201, DRB436A2102, regardless of current age
3. Parent study (or cohort of parent study) is planned to be closed
4. Patient has demonstrated treatment compliance, as assessed by the Investigator, within the parent study protocol requirement(s).
5. Willingness and ability to comply with scheduled visits, treatment plans and any other study procedures.
For Subjects Entering the Treatment Period
6. Patient is currently receiving treatment with dabrafenib/trametinib monotherapy or combination within a Novartis Sponsored Drug Development study.
7. In the opinion of the Investigator, the subject is likely to benefit from continued treatment.
8. Does not require treatment with prohibited concomitant medications.

Exclusion criteria

1. Patient has participated in a combination trial where dabrafenib and/or trametinib was dispensed in combination with another study medication. (Exception: Patients who were on the chemotherapy arm of the CDRB436G2201 study are eligible for this study after crossing over into the experimental treatment arm of the CDRB436G2201 study or have discontinued the study treatment and are now in follow-up)
2. Patient has permanently discontinued from study treatment in the parent protocol due to any reason.
3. Treatment with dabrafenib and/or trametinib for the patient*s indication is approved for marketing and the appropriate dosage form is commercially available and reimbursed in the local country

4. Patient currently has unresolved drug related severe toxicities for which dabrafenib and/or trametinib dosing has been interrupted in the parent study. If the patient should meet criteria to resume treatment on the parent protocol then they may be eligible for enrolment in this study.

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):	17-01-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

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:	26-10-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-12-2022
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	26-05-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-06-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-09-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-09-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-10-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-10-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	28-11-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-12-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-04-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-04-2024
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	CTIS2023-509276-42-00
EudraCT	EUCTR2018-004459-19-NL
ClinicalTrials.gov	NCT03975829
CCMO	NL81911.041.22