A phase 3, randomized, placebo-controlled, double-blind study of vimseltinib to assess the efficacy and safety in patients with tenosynovial giant cell tumor (MOTION)

Published: 09-08-2021
Last updated: 25-09-2024

This study has been transitioned to CTIS with ID 2024-513624-42-00 check the CTIS register for the current data. Primary Objective: • To evaluate anti-tumor activity of vimseltinib using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56439

Source
ToetsingOnline

Brief title
MOTION

Condition

- Other condition
- Synovial and bursal disorders
- Soft tissue neoplasms benign

Synonym
rare tumor arising from the joints, Tenosynovial Giant Cell Tumor

Health condition

Advanced tumors

Research involving
Human

Sponsors and support

Primary sponsor: Deciphera Pharmaceuticals, LLC
Source(s) of monetary or material Support: Deciphera Pharmaceuticals;LLC

Intervention

Keyword: pigmented villonodular synovitis, tenosynovial giant cell tumor, Vimseltinib

Outcome measures

Primary outcome

Primary Endpoint:

• Objective response rate (ORR, including complete response [CR] and partial response [PR]) per RECIST v1.1 at Week 25

Secondary outcome

Key Secondary Endpoints:

• ORR per TVS at Week 25

• Change from baseline in active ROM of the affected joint, relative to a reference standard, at Week 25

• Change from baseline in the Patient-reported Outcomes Measurement Information System (PROMIS) physical function score at Week 25

• Change from baseline in the Worst Stiffness numeric rating scale (NRS) score at Week 25

• Change from baseline in EQ-VAS (EuroQol Visual Analogue Scale) at Week 25

• Response of at least a 30% improvement in the mean Brief Pain Inventory (BPI) Worst Pain NRS score without a 30% or greater increase in narcotic analgesic

use at Week 25

Other Secondary Endpoints:

• ORR per RECIST v1.1

• ORR assessed by mRECIST at Week 25

• Duration of response (DOR; time from first PR or CR to disease progression or death) assessed using RECIST v1.1, TVS, and mRECIST

• Incidence of treatment-emergent adverse events (TEAEs), treatment-emergent serious adverse events, related TEAEs, dose reductions, dose interruptions, and discontinuation of study drug due to adverse event

• Changes from baseline in laboratory parameters, electrocardiograms (ECGs), and vital signs

Study description

Background summary

TGCT is a rare tumor arising from the synovium of joints, bursae, and tendon sheaths. Translocation of the CSF1 gene has been identified in TGCT patients, resulting in overproduction of CSF1 and recruitment of CSF1R-positive inflammatory cells in the affected joint.

Vimseltinib (DCC-3014) is an oral, small molecule, selective inhibitor of colony-stimulating factor 1 receptor (CSF1R) developed by the Sponsor using its proprietary switch control kinase inhibitor technology platform. CSF1R is a tyrosine kinase receptor expressed predominantly on monocytes and macrophages. Vimseltinib binds to the pocket controlling the conformation of the CSF1R kinase domain and locks the kinase domain in the inactive form. In vitro studies have demonstrated vimseltinib to be a potent and selective inhibitor of CSF1R kinase. Vimseltinib is currently being evaluated for the treatment of advanced solid tumors and tenosynovial giant cell tumor (TGCT) in an ongoing Phase 1/2 clinical development study (Study DCC-3014-01-001; NCT03069469; NL70948.058.19).

Study objective

This study has been transitioned to CTIS with ID 2024-513624-42-00 check the CTIS register for the current data.

Primary Objective:
• To evaluate anti-tumor activity of vimseltinib using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 by blinded independent radiological review (IRR)
Secondary Objectives:
• To assess anti-tumor activity of vimseltinib using tumor volume score (TVS) and modified RECIST (mRECIST) by blinded IRR
• To assess the effects of vimseltinib on range of motion (ROM)
• To assess the effects of vimseltinib on physical function, worst stiffness, worst pain, and quality of life (QoL) using patient-reported outcome (PRO) measures
• To assess safety and tolerability of vimseltinib

Study design

This is a multicenter, randomized, placebo-controlled study of vimseltinib in patients with tenosynovial giant cell tumor (TGCT), consisting of 2 parts: Part 1 is double blinded and Part 2 is open label. Symptomatic patients with histologically confirmed TGCT for whom surgical resection will potentially cause worsening functional limitation or severe morbidity will be eligible. Patients who received anti-colony-stimulating factor 1/colony-stimulating factor 1 receptor (CSF1/CSF1R) therapy previously (except for imatinib or nilotinib) will be excluded. The study will evaluate efficacy, safety, clinical outcome assessments, pharmacokinetics (PK), and pharmacodynamics of vimseltinib in this population.

The study will consist of a 42-day screening period prior to the first dose of study drug, a Part 1 double-blinded treatment period of 24 weeks (referred to in 28-day cycles) and a Part 2 open-label period until Week 49. Participants will continue treatment after Week 49 during the extension period. There will also be an End-of-Treatment (EOT) Visit within 7 days after the decision to stop study drug, a Safety Follow-up visit 30 days (±5 days) after the last dose of study drug, and a Disease Follow-up period of up to 2 years or until initiation of new TGCT treatment or surgery, whichever occurs first. Participants will be allowed to undergo surgical resection only after completion of Part 1.

Approximately 120 participants will be randomized in a 2:1 ratio to receive either vimseltinib at the dose of 30 mg twice weekly (biw) (n=80) or placebo (n=40) for 24 weeks. Randomization will be stratified for tumor location (lower limb/all other) and region (U.S./non-U.S.).

At Week 25, the primary and secondary endpoints will be assessed, and participants randomized to placebo in Part 1 will have the option to crossover

and receive open-label vimseltinib in Part 2 upon completion of Part 1. Participants randomized to placebo in Part 1 with confirmed disease progression by blinded IRR before Week 25 are eligible for early entry into Part 2. Participants randomized to vimseltinib in Part 1 with confirmed disease progression by IRR before Week 25 will discontinue from study, while those without confirmed disease progression by IRR before Week 25 will continue to receive vimseltinib in Part 2 upon completion of Part 1.

Anti-tumor activity will be assessed by RECIST v1.1. Tumor volume score and mRECIST will be used as additional assessments of anti-tumor activity. Range of motion assessments will be performed and PRO measures will be collected. Safety will be assessed using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Correlation between efficacy or safety with PK and pharmacodynamics will be explored.

Intervention

Study Drug, Dosage, and Route of Administration: Vimseltinib 30 mg or matching placebo twice weekly will be administered as oral capsules on an empty stomach, at least 1 hour before and no sooner than 2 hours after ingestion of food.

Study burden and risks

Side effects associated with the vimseltinib
Very common
• Periorbital oedema (Swelling around the eyes due to accumulation of fluid) (28%)
• Increased levels of an enzyme produced by the liver in blood, which in rare cases, may indicate liver injury (23%)
• Fatigue (23%)
• Increased levels of an enzyme produced by the heart or muscle in blood, which may indicate muscle injury/inflammation, rarely heart injury (22%)
• An increase in enzymes produced by the pancreas in the blood which may indicate pancreatic injury or inflammation (17%)
• Diarrhea (12%)
• Nausea (12%)
• Face edema (Swelling of the face due to accumulation of fluid) (12%)
• Itching (12%)
Side effects reported in more than 3 patients (5%) but less than 6 patients (10%):
• Peripheral Edema (swelling of the arms and/or legs due to accumulation of fluid) (8%)
• Rash (8%)
• Muscle pain or muscle aches (7%)
• Abdominal pain (5%)
• Headache (5%)

• Vomiting (5%)

Of all the patients who have received vimseltinib, approximately 5% stopped the study treatment because
of side effects related to the study drug.

Possible Drug Interactions
Vimseltinib may interfere with other drugs that you are taking. Likewise, other drugs may interfere with vimseltinib. Allergic reactions may occur.

Blood draws
Blood draws may cause injection site swelling and/or pain, dizziness, lightheadedness, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count). Fasting may cause your blood sugar to drop. You may feel tired, hungry, and/or nauseous. If you have diabetes, it is important to talk to your doctor about managing your blood sugar while fasting.

MRI Risks
MRI scans use radio frequency waves (like those in an AM/FM radio) and a powerful magnet to take pictures of inside the body. An MRI scanner is a large tube, open at both ends. During the scan, the subject will lie inside the tube. The dye used for MRIs may cause headache, nausea, stomach pain, and convulsions. There is the possibility of a severe allergic reaction that may be life threatening in which may lead to difficulty breathing and a decreased blood pressure.

ECG Risks
The tape used to adhere the electrodes to the skin may cause some redness and/or swelling.

Pregnancy risks
Vimseltinib can cause harm to an unborn baby when administered to pregnant women. The effects of vimseltinib on the reproductive system (sperm, eggs), conception, and lactation are not known.

Phototoxicity risks
Strong sunlight, sunlamps, and other sources of ultraviolet radiation (a type of light) for the duration of the study to prevention of phototoxicity.

Tumor biopsy
The risks associated with a tumor biopsy may include bleeding, pain, and infection. Once anesthesia wears off, you may feel pain that can last for several days. Risks associated with local anesthesia include pain during administration, prolonged numbness, infection, or a reaction to the anesthesia.

Unknown Risks
There may be risks to subjects that are currently not known or cannot be predicted. Their condition may worsen, remain the same, or improve as a result of participating in this research study. Subjects should tell the study doctor or staff about all problems, illnesses, or injuries that happen to them during the study, even if they think they are not related to their taking part in this study. Subjects might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. New ones could happen to them. They should tell the study doctor or study staff right away if they have any problems.

Benefit:
Treatment with the study drug may lead to a partial or complete shrinkage of the tumor. Anti-tumor activity data as of 07 Jun 2021 demonstrated an objective response rate (ORR) of 50% in 32 patients across 3 dose escalation cohorts, and an ORR of 42% (all Partial response) in 19 patients in expansion Cohort A at the recommended Phase 2 dose, which is also the selected Phase 3 dose. Objective responses were generally achieved after at least 2 cycles of treatment and responses were durable.

Contacts

Public
Deciphera Pharmaceuticals, LLC

Smith Street 200
Waltham 02451
US
Scientific
Deciphera Pharmaceuticals, LLC

Smith Street 200
Waltham 02451
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Participants must meet all of the following criteria to be eligible to enroll in the study:
1. Male or female participants >=18 years of age
2. Histologically confirmed diagnosis of TGCT (formerly known as pigmented villonodular synovitis [PVNS] or giant cell tumor of the tendon sheath [GCT-TS]). Tumor biopsy to confirm TGCT diagnosis will be required if no histology/pathology is available
a. Participants should have TGCT in a single joint and must have TGCT in joints where ROM assessments can be assessed
3. Disease for which surgical resection will potentially cause worsening functional limitation or severe morbidity as judged by surgical consultation or a multidisciplinary tumor board
4. Symptomatic disease with at least moderate pain or at least moderate stiffness (defined as a score of 4 or more, with 10 describing the worst condition) within the screening period and documented in the medical record
5. Participants should complete 14 consecutive days of questionnaires during the screening period and must meet minimum requirements outlined in Table 4
6. An analgesic regimen, if used, needs to be stable (ie, no change in dose) as judged by the Investigator for at least 2 weeks prior to the first dose of study drug
7. Measurable disease per RECIST v1.1 with at least one lesion having a minimum size of 2 cm, as assessed from magnetic resonance imaging (MRI) scans by a central radiologist
8. Adequate organ function and bone marrow reserve as indicated by the following laboratory assessments performed within 21 days prior to the first dose of study drug:
a. Bone marrow function: absolute neutrophil count (ANC) >=1500/µL; hemoglobin >=10 g/dL; platelet count >=lower limit of normal (LLN)
b. Hepatic function: total serum bilirubin <=upper limit of normal (ULN); serum aspartate aminotransferase (AST)/ alanine aminotransferase (ALT) <=ULN
c. Renal function: creatinine clearance >=50 mL/min based either on urine collection or Cockcroft-Gault estimation
d. Electrolytes >=LLN for: potassium, magnesium, and calcium
9. Able to take oral medication
10. Participants of reproductive potential must:
a. Have a negative serum beta human chorionic gonadotropin (β hCG) pregnancy test at screening (female participants)

b. Agree to follow the contraception requirements outlined in the protocol
11. The participant is capable of understanding and complying with the protocol and has signed the informed consent form (ICF). A signed ICF must be obtained before any study-specific procedures are performed
12. Willing and able to complete the PRO assessments on an electronic device

Exclusion criteria

Participants meeting any of the following criteria will be excluded from the study:
1. Previous use of systemic therapy (investigational or approved) targeting CSF1 or CSF1R including vimseltinib; previous therapy with imatinib and nilotinib is allowed
2. Treatment for TGCT, including investigational therapy, during the screening period.
NOTE: Participants may not be part of an ongoing or have prior participation in a non-TGCT investigational drug study within 30 days of screening. Ongoing participation in a noninterventional study (including observational studies) is permitted.
3. Known metastatic TGCT or other active cancer that requires concurrent treatment (exceptions will be considered on a case-by-case basis depending on tumor type, stage, location, planned treatment, and expected recovery after discussion and approval by Sponsor)
4. Baseline prolongation of the QT interval corrected by Fridericia's formula (QTcF) based on repeated demonstration of QTcF >450 ms in males or >470 ms in females or history of long QT syndrome
5. Receive concurrent treatment with any prohibited medications
• Acetaminophen usage exceeding 3 g/day
• Proton-pump inhibitors taken within 4 days prior to the first dose of study drug
• Medications that are breast cancer resistance protein (BCRP) or organic cation transporter 2 (OCT2) substrates taken within at least 4 days or 5×half-life (whichever is longer) prior to the first dose of study drug
• Medications with a known risk of prolonging the QT interval within at least 14 days or 5×half-life (whichever is longer) prior to the first dose of study drug (see Appendix 1)
• Prophylactic use of myeloid growth factors (eg, granulocyte colony-stimulating factor [G CSF], granulocyte macrophage-colony-stimulating factor [GM-CSF])
6. Major surgery within 14 days of the first dose of study drug; following major surgeries >14 days prior to the first dose of study drug, all surgical wounds must be healed and free of infection or dehiscence
7. Any clinically significant comorbidities, such as significant concomitant arthropathy not related to TGCT in the affected joint, or any other serious medical or psychiatric condition(s), known current alcohol abuse, which in the

judgment of the Investigator, could compromise compliance with the protocol, interfere with the interpretation of study results, or predispose the participant to safety risks
8. Active liver or biliary disease including nonalcoholic steatohepatitis (NASH) or cirrhosis
9. Malabsorption syndrome or other illness that could affect oral absorption as judged by the Investigator
10. Known active human immunodeficiency virus (HIV), acute or chronic hepatitis B, acute or chronic hepatitis C, or known active mycobacterium tuberculosis infection
11. If female, the participant is pregnant or breastfeeding
12. Known allergy or hypersensitivity to any component of the study drug
13. Contraindication to MRI

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-03-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	vimseltinib
Generic name:	N/A

Ethics review

Approved WMO Date:	09-08-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	02-03-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	06-08-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-01-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	30-01-2023
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	01-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	16-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	CTIS2024-513624-42-00
EudraCT	EUCTR2020-004883-25-NL
CCMO	NL77575.058.21