A Multicenter, Open-label, Randomized Phase 2 Study to Compare the Efficacy and Safety of Lenvatinib in Combination with Ifosfamide and Etoposide versus Ifosfamide and Etoposide in Children, Adolescents and Young Adults with Relapsed or Refractory Osteosarcoma (OLIE)

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Primary ObjectiveTo evaluate whether lenvatinib in combination with ifosfamide and etoposide (Arm A) is superior to ifosfamide and etoposide (Arm B) in improving progression-free survival (PFS) by independent imaging review [IIR] using Response...

Ethical review	Approved WMO
Status	Completed
Health condition type	Skeletal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON49371

Source
ToetsingOnline

Brief title
OLIE

Condition

- Skeletal neoplasms malignant and unspecified

Synonym
cancer in the bone, relapsed or refractory osteosarcoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: lenvatinib, osteosarcoma, refractory, relapsed

Outcome measures

Primary outcome

PFS (progression-free survival) by IIR is defined as the time from the date of randomization to the date of the first documentation of PD or death (whichever occurs first) as determined by IIR using RECIST 1.1.

Secondary outcome

-PFS-4m rate (progression-free survival rate at 4 months) by IIR is defined as the percentage of subjects who are alive and without PD at 4 months from the randomization date as determined by IIR of radiological imaging using RECIST 1.1. The PFS-4m rate is estimated using the Kaplan-Meier (K-M) method.

-PFS-1y rate (progression-free survival rate at 1 year) by IIR is defined as the percentage of subjects who are alive and without PD at 1 year from the randomization date as determined by IIR of radiological imaging using RECIST 1.1. The PFS-1y rate is estimated using the K-M method.

-Overall survival (OS) is defined as the time from the date of randomization to the date of death from any cause. Subjects who are lost to follow-up and those

who are alive at the date of data cutoff for the primary analysis, will be censored at the date the subject was last known to be alive, or date of data cutoff for the primary analysis, whichever occurs first. Overall survival rate at 1 year (OS-1y) will be estimated using the K-M method.

-Objective response rate by IIR at 4 months (ORR-4m) is defined as the proportion of subjects who have best overall response of complete response (CR) or partial response (PR) as determined by IIR using RECIST 1.1 within the first 4 months.

-Objective response rate (ORR) by IIR is defined as the proportion of subjects who have best overall response of complete response (CR) or partial response (PR) as determined by IIR using RECIST 1.1.

-Safety will be assessed summarizing the incidence of treatment-emergent adverse events (TEAEs) and SAEs together with all other safety parameters.

-Assessment of population-based PK parameters of lenvatinib.

-Score changes from baseline for all PedsQL scales including Generic Core Scales and Cancer Module. Scores will be calculated for total generic score, total cancer score, each physical function subscale including physical health, psychosocial health, emotional function, social function, school/work function in the Generic Core Scales, and each subscales in the cancer module.

-Palatability and acceptability of the suspension formulation of lenvatinib in subjects receiving the suspension formulation in the study will be assessed using the Palatability Questionnaire

Study description

Background summary

Osteosarcoma is the most commonly diagnosed primary malignancy of the bone in children and young adults, and accounts for approximately 5% of childhood tumours, with an estimated annual incidence of 4.4 cases per 1 million in people younger than 24 years. Osteosarcoma occurs predominantly in adolescents and young adults. The median age at diagnosis is 20 years, with the incidence peaking at 15 to 19 years of age.

Current treatment options for patients with osteosarcoma in or after second-line treatment are limited and the prognosis is often poor. There has been no substantial progress in the treatment of osteosarcoma since the 1980s. The second-line treatment for recurrent disease consists of chemotherapy and / or surgical resection. The role of second-line chemotherapy for recurrent osteosarcoma is much less well defined than that of surgery, and there is no general accepted standard regime.
As per the European Society for Medical Oncology (ESMO) guidelines for bone sarcoma,treatment options for recurrent osteosarcoma include ifosfamide ± etoposide ± carboplatin, and other active drugs. Preferred regimens for second-line therapy per the National Comprehensive Cancer Network (NCCN) bone sarcoma guidelines include ifosfamide (high dose) with or without etoposide, regorafenib, sorafenib, and sorafenib plus everolimus. In the event of subsequent relapse, the NCCN guidelines and ESMO guidelines strongly encourage participation in clinical studies. Otherwise, patients with disease progression or relapse after second-line therapy are managed with surgical resection, palliative radiotherapy, or best supportive care (refer to introduction section of the protocol).

Lenvatinib is an anticancer agent authorised to treat progressive or advanced thyroid cancer in adults. Lenvatinib belongs to a type of anti-cancer treatments known as receptor tyrosine kinase (RTK) inhibitors, which are involved in the growth of cells and the development of new blood vessels that supply them.
Previous studies have shown that Lenvatinib has activity in solid tumours, including relapsed or refractory osteosarcoma, and radioiodine-refractory differentiated thyroid carcinoma and is tolerable in children, adolescents and young adults.
Combining Lenvatinib with Ifosfamide and etoposide may have more activity against relapsed or refractory osteosarcoma than when used alone.

Study objective

Primary Objective

To evaluate whether lenvatinib in combination with ifosfamide and etoposide (Arm A) is superior to ifosfamide and etoposide (Arm B) in improving progression-free survival (PFS) by independent imaging review [IIR] using Response Evaluation Criteria In Solid Tumors [RECIST 1.1], in children, adolescents, and young adults with relapsed or refractory osteosarcoma.

Secondary Objectives
The secondary objectives of the study are to:
1. Compare difference in PFS rate at 4 months (PFS-4m) between the 2 treatment arms per IIR
2. Compare difference in PFS rate at 1 year (PFS-1y) between the 2 treatment arms per IIR
3. Compare difference in overall survival (OS) and OS rate at 1 year (OS-1y) between the 2 treatment arms
4. Compare difference in objective response rate at 4 months (ORR-4m) between the 2 treatment arms per IIR
5. Compare difference in objective response rate (ORR) between the 2 treatment arms per IIR
6. Compare difference in safety and tolerability between the 2 treatment arms
7. Characterize the pharmacokinetics (PK) of lenvatinib, when administered in combination with ifosfamide and etoposide
8. Compare difference in health-related quality of life (HRQoL) as assessed by using the Pediatric Quality of Life Inventory (PedsQL) Generic Core Scales and Cancer Module between the 2 treatment arms
9. Assess the palatability and acceptability of the suspension

The exploratory objectives of the study are to:
1. Explore difference in duration of response (DOR), disease control rate (DCR), and clinical benefit rate (CBR) between the 2 treatment arms per IIR and investigator assessment
2. Explore difference in PFS, PFS-4m, PFS-1y, ORR-4m, and ORR between the 2 treatment arms per investigator assessment
3. Compare between the 2 treatment arms:
- the proportion of subjects who achieve complete removal of baseline lesion(s)
- the proportion of subjects with unresectable baseline lesion(s) that are converted to resectable
4. Investigate the relationship between tumor biomarkers and clinical response and toxicity of lenvatinib in combination with ifosfamide and etoposide

Study design

E7080-G000-230 is a multicenter, randomized, open-label, parallel-group, Phase 2 study to compare the efficacy and safety of lenvatinib in combination with ifosfamide and etoposide versus ifosfamide and etoposide in children, adolescents, and young adults with relapsed or refractory osteosarcoma. Approximately 72 eligible subjects will be randomized to 1 of the following 2 treatment arms in a 1:1 ratio within the strata:

- Arm A: lenvatinib 14 mg/m2 (orally, once daily) plus ifosfamide 3000 mg/m2/day (intravenously[IV], Day 1 to Day 3 of each cycle for a total of up to 5 cycles) and etoposide 100 mg/m2/day(IV, Day 1 to Day 3 of each cycle for a total of up to 5 cycles)
-Arm B: ifosfamide 3000 mg/m2/day (IV, Day 1 to Day 3 of each cycle for a total of up to5 cycles) and etoposide 100 mg/m2/day (IV, Day 1 to Day 3 of each cycle for a total of up to 5cycles)
Randomization will follow a predefined randomization scheme based on the following stratification factors: time to first relapse/refractory disease (early [<18 months] or late [>=18 months]) and age (<18 and >=18 years).
The Sponsor will closely monitor enrollment, to ensure that a minimum of 36 subjects are <17 years of age at the time of informed consent.
The study will be conducted in 3 Phases: a Prerandomization Phase, a Randomization Phase, and an Extension Phase.
The Extension Phase will consist of 2 periods: Treatment Period and Follow-up Period.
There is an optional Lenvatinib Crossover for Subjects in Arm B only.

Intervention

Test Arm (Arm A): Lenvatinib + Ifosfamide + Etoposide
Lenvatinib 14 mg/m2, orally administered once daily in each 21-day cycle. Lenvatinib is provided as hard capsules containing 1 mg, 4 mg, or 10 mg lenvatinib. An extemporaneous suspension of lenvatinib capsules should be used for subjects unable to swallow capsules. After adjustment for BSA, the daily dose cannot exceed 24 mg QD.
Ifosfamide 3000 mg/m2/day, IV, for 3 consecutive days (Day 1 to 3), every 21 days, for a maximum of 5 cycles.
Etoposide 100 mg/m2/day, IV, for 3 consecutive days (Day 1 to 3) , every 21 days, for a maximum of 5 cycles.
Treatment with lenvatinib will continue in 21-day cycles after chemotherapy is discontinued, until disease progression, development of unacceptable toxicity, subject request, withdrawal of consent, or discontinuation of study by the sponsor.

In case the study is discontinued by the sponsor, the sponsor will provide study drug (outside the study) for subjects who have not met the criteria for study drug discontinuation.

Control Arm (Arm B): Ifosfamide + Etoposide
Ifosfamide 3000 mg/m2/day, IV, daily for 3 consecutive days (Day 1 to 3), every 21 days, for a maximum of 5 cycles.
Etoposide 100 mg/m2/day, IV, daily for 3 consecutive days (Day 1 to 3), every 21 days, for a maximum of 5 cycles.

Optional Lenvatinib Crossover (for Subjects in Arm B Only):
Subjects in Arm B with disease progression per RECIST 1.1 may be eligible for

optional treatment with lenvatinib±chemotherapy.

Study burden and risks

The participants are asked to undergo the following procedures: Physical examination, questionnaires (palatability quality of life), Tanner staging, ECG, ECHO, Blood and urine samples, Pregnancy test, CT/MRI scans, X-ray, study drug administration. These can be accomapnied by risks and discomfort. An overview is provided in the Informed Consent Form.

Lenvatinib can have certain risks. A full overview of side effects is provided in the Informed Consent Form.

The most common serious and potentially life-threatening side effects of Lenvatinib are:
-Stroke, mini-stroke or bleeding in the brain
-Blood clot in the legs or lungs (pulmonary embolism)
-Heart problems, heart palpitations or heart attack
-Fistula formation or bowel perforation
-Bleeding inside the body particularly from the gut
-Dehydration and kidney failure
-Heart failure
-Liver damage or failure
-Hepatic encephalopathy,

Subjects will be carefully monitored for side effects.

The current therapeutic options for the eligible patients are limited and the prognosis is often poor. There has been no substantial progress in the treatment of osteosarcoma since the 1980s. Current treatment utilizes multi-agent chemotherapy and surgical resection of all clinically detectable disease. Second-line treatment for relapsed disease consists of chemotherapy and/or surgical resection. The role of second-line chemotherapy for recurrent osteosarcoma is much less well defined than that of surgery, and there is no accepted standard regimen.
In the event of subsequent relapse, the NCCN guidelines and ESMO guidelines strongly encourage participation in clinical studies. Otherwise, patients with disease progression or relapse after second-line therapy are managed with surgical resection, palliative radiotherapy, or best supportive care.

Pediatric solid tumors are highly vascularized. Angiogenesis and vasculogenesis are the fundamental processes by which new blood vessels are formed. As with normal tissue, the growing tumor requires an extensive network of capillaries to provide the necessary nutrients and oxygen. Moreover, the new intratumor blood vessels offer a way for tumor cells to enter the circulation and metastasize to distant organs and thus play an indispensable role in solid tumor growth and metastasis. Thus, inhibition of angiogenesis is a viable

target for anticancer therapy. Moreover, vascular normalisation allows reoxygenation, hence the addition of an anti-VEGF to chemotherapy may result in increased uptake of drugs into tumor tissue (Tuettenberg, et al., 2006).

E7080 (lenvatinib) is a potent multiple receptor tyrosine kinase (RTK) inhibitor (RTKI) that selectively inhibits VEGF receptors, VEGFR1 (FLT1), VEGFR2 (KDR), and VEGFR3 (FLT4), in addition to other pro-angiogenic and oncogenic pathway-related RTKs, including fibroblast growth factor (FGF) receptor (FGFR) 1-4, PDGF receptor alpha (PDGFRα), KIT, and RET. Therefore, lenvatinib exerts it*s in vivo antitumoural activity based on multiple mechanisms involved in and through effects related to angiogenesis (including reversion of resistance) and the tumor microenvironment, as well as direct inhibitory action on the tumour cells. Recent studies have also demonstrated lenvatinib*s immunomodulatory activity in the tumor microenvironment. This includes decreases in immunosuppressive tumor-associated macrophages, activated cytotoxic T cell increases, and activation of interferon-gamma signaling. These all contribute to lenvatinib*s antitumor activity in immunocompetent mice.

Data from a previous study [Study 207] have shown that patients with osteosarcoma may benefit from treatment with lenvatinib. In the single agent expansion cohort in relapsed/refractory osteosarcoma, (n=31* Cohort 2B), 9 of 28 evaluable patients (32.1%) achieved progression-free survival (PFS) at 4 months (PFS-4m), median PFS was 3.0 months (95% CI: 1.8, 5.5). Two out of 29 subjects (6.9%) with measurable disease had a partial response (PR). Overall treatment with lenvatinib in combination with ifosfamide and etoposide in this patient population was associated with a manageable safety profile, and no unexpected toxicities were observed.

Contacts

Public
Eisai

Mosquito Way _
Hatfield AL10 9SN
GB
Scientific
Eisai

Mosquito Way _
Hatfield AL10 9SN
GB

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)
Elderly (65 years and older)

Inclusion criteria

1. Histologically or cytologically confirmed diagnosis of high grade osteosarcoma.
2. Refractory or relapsed osteosarcoma after 1 to 2 prior lines of systemic treatments.
3. Measurable or evaluable disease per RECIST 1.1 that meets the following criteria:
- Measurable disease is defined as a lesion with a minimum size (by long axis) of 10 mm using computed tomography/magnetic resonance imaging (CT/MRI) (lymph nodes must be accurately measurable with a minimum size [by short axis] of 15 mm).
- Lesions that have had external beam radiotherapy (EBRT) or locoregional therapies such as radiofrequency (RF) ablation must have subsequently grown unequivocally to be deemed a target lesion.
- Any other non-measurable lesions will be considered evaluable disease.
4. Aged 2 years to <=25 years at the time of informed consent.
5. Life expectancy of 12 weeks or more.
6. Lansky play score >=50% or Karnofsky Performance Status score >= 50%. Use Karnofsky for subjects >=16 years of age and Lansky for subjects <16 years of age. Subjects who are unable to walk because of paralysis, but who are able to perform Activities of Daily Living (ADL) while wheelchair bound, will be considered ambulatory for the purpose of assessing the performance score.
7. Adequate bone marrow function as evidenced by:
a. absolute neutrophil count (ANC) >=1.5×10^9/L. (subjects with bone marrow involvement should have ANC >=0.8×10^9/L and leucocyte count >=1×10^9/L).
b. hemoglobin >=8.0 g/dL (a hemoglobin of <8.0 g/dL is acceptable if it is

corrected by growth factor or transfusion before Cycle 1 Day 1).
c. platelet count >=100×10^9/L. 8. Adequate blood coagulation function defined by International
Normalized ratio or prothrombin time (INR/PT) and activated partial thromboplastin time or partial thromboplastin time (aPTT/PTT) <=1.5 unless participant is receiving anticoagulant therapy, as long as INR/PT and aPTT/PTT are within therapeutic range of intended use of anticoagulants.
9. Adequate liver function as evidenced by:
a. Bilirubin <=1.5 times the upper limit of normal (ULN).
b. Alanine aminotransferase (ALT), and aspartate aminotransferase (AST) <=3×ULN (in the case of liver metastases <=5×ULN).
10. Adequate renal function as evidenced by:
a. Serum creatinine based on age/gender as below. If serum creatinine is greater than maximum serum creatinine for age/gender as shown in the table within the protocol page 5, then creatinine clearance (or radioisotope glomerular filtration rate [GFR]) must be >70 mL/min/1.73 m2.
b. Urine dipstick <2+ for proteinuria. Subjects who have >=2+ proteinuria on dipstick urinalysis should undergo a spot protein-creatinine (P/C) ratio test that should be Grade <2 per Common Terminology Criteria for Adverse Events (CTCAE) v5.0 and if possible perform a 24-hour urine
collection (children and adolescents <=12 years of age must have <=500 mg of protein/24 hours and subjects >12 years of age must have <=1 g of protein/24 hours).
c. No clinical evidence of nephrotic syndrome.
11. Adequate cardiac function as evidenced by left ventricular ejection fraction >=50% at baseline as determined by echocardiography or multigated acquisition (MUGA) scan.
12. Adequately controlled blood pressure (BP) with or without antihypertensive medications, defined as:
a. BP <95th percentile for sex, age, and height/length at screening (as per National Heart Lung and Blood Institute guidelines) and no change in antihypertensive medications within 1 week prior to Cycle 1 Day 1.
Subjects >18 years of age should have BP <=150/90 mm Hg at screening and no change in antihypertensive therapy within 1 week prior to Cycle 1 Day 1.
13. Washout before Cycle 1 Day 1 of 3 weeks in case of prior chemotherapy, 6 weeks if treatment
included nitrosoureas; 4 weeks for definitive radiotherapy, 2 weeks for palliative radiotherapy; and 3 months from high-dose chemotherapy and stem cell rescue. For all other anti-cancer therapies, washout before Cycle 1 Day 1 of at least 5 half-lives (or at least 28 days, whichever is
shorter). Subjects must have recovered (to Grade <=1, except for alopecia, ototoxicity, and Grade <=2 peripheral neuropathy, per CTCAE v5.0) from the acute toxic effects of all prior anticancer therapy before Cycle 1 Day 1.
14. Must have no prior history of lenvatinib treatment.
15. Written and signed informed consent from the parent(s) or legal guardian and assent from the minor subject. Written informed consent from subjects >=18 years.

16. Willing and able to comply with the protocol, scheduled follow-up, and management of toxicity as judged by the investigator.

Exclusion criteria

1. Any active infection or infectious illness unless fully recovered prior to Cycle 1 Day 1.
2. Subjects with central nervous system metastases are not eligible, unless they have completed local therapy and have discontinued the use of corticosteroids for this indication at least 2 weeks before C1D1
3. Active second malignancy within 2 years prior to enrollment
4. Any medical or other condition that in the opinion of the investigator(s) would preclude the subject's participation in a clinical study.
5. Has had major surgery within 3 weeks prior to Cycle 1 Day 1.
6. Known hypersensitivity to any component(s) of the study drugs (lenvatinib, ifosfamide, and etoposide, or their ingredients).
7. Currently receiving any investigational drug or device in another clinical study or within 28 days prior to Cycle 1 Day 1.
8. A clinically significant ECG abnormality, including a marked baseline prolonged QT or QTc interval (eg, a repeated demonstration of a QTc interval > 480 msec).
9. Has clinically significant cardiovascular disease within 6 months from first dose of study intervention, including New York Heart Association Class III or IV congestive heart failure, unstable angina, myocardial infarction, cerebral vascular accident, or cardiac arrhythmia associated
with hemodynamic instability. Note: Medically controlled arrhythmia would be permitted.
10. Gastrointestinal malabsorption, gastrointestinal anastomosis, or any other condition that in the opinion of the investigator might affect the absorption of lenvatinib.
11. Pre-existing Grade >=3 gastrointestinal or non-gastrointestinal fistula.
12. Gastrointestinal bleeding or active hemoptysis (bright red blood of at least * teaspoon) within 3 weeks prior to Cycle 1 Day 1.
13. Radiographic evidence of intratumoral cavitation, encasement, or invasion of a major blood vessel. Additionally, the degree of proximity to major blood vessels should be considered for exclusion because of the potential risk of severe hemorrhage associated with tumor shrinkage/necrosis after lenvatinib therapy.
14. History of ifosfamide-related Grade >=3 nephrotoxicity or encephalopathy.
15. Evidence of clinically significant disease (eg, cardiac, respiratory, gastrointestinal, renal disease) that in the opinion of the investigator(s) could affect the subject's safety or interfere with the study assessments.
16. Known to be human immunodeficiency virus (HIV) positive. Note: HIV testing is required at screening only when mandated by local authority.
17. Known active Hepatitis B (eg, HBsAg reactive) or Hepatitis C (eg, HCV RNA

[qualitative] is detected). Note: Testing for Hepatitis B or Hepatitis C is required at screening only when mandated by local health authority.
18. Females who are breastfeeding or pregnant at Screening or Baseline (as documented by a positive beta-human chorionic gonadotropin [ßhCG]) (human chorionic gonadotropin [hCG]) test with a minimum sensitivity of 25 IU/L or equivalent units of ß-hCG /hCG]). A separate baseline assessment is required if a negative screening pregnancy test was obtained more than 72 hours before the first dose of any study drug.
19. Females of childbearing potential* who:
- Do not agree to use a highly effective method of contraception for the entire study period and for 28 days after lenvatinib discontinuation or 12 months after etoposide and ifosfamide discontinuation, ie:
* total abstinence (if it is their preferred and usual lifestyle)
* an intrauterine device (IUD) or intrauterine hormone-releasing system (IUS)
* A contraceptive implant
* an oral contraceptive **(with additional barrier method)
OR
- Do not have a vasectomized partner with confirmed azoospermia.
* All post pubertal females will be considered to be of childbearing potential unless they have early menopause (amenorrheic for at least 12 consecutive months, in the appropriate age group, and without other known or suspected cause) or have been sterilized surgically (ie, bilateral tubal ligation, total hysterectomy, or bilateral oophorectomy, all with surgery at least 1 month before dosing), or are pre-menarcheal (Tanner Stage 1-3).
**Must be on stable dose of the same oral hormonal contraceptive product for at least 4 weeks before dosing with study drug(s) and for the duration of the study.
20. Males who have not had a successful vasectomy (confirmed azoospermia) or if they and their female partners do not meet the criteria above (ie, not of childbearing potential or practicing highly effective contraception throughout the study period and for 28 days after lenvatinib discontinuation or 6 months after discontinuation of etoposide and ifosfamide). No sperm donation is allowed during the study period and for 28 days after lenvatinib discontinuation or 6 months after discontinuation of etoposide and ifosfamide
21. A contraindication to any of the study drugs (lenvatinib, ifosfamide, and etoposide) per local prescribing information

Study design

Design

Study phase:	2
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	26-07-2021
Enrollment:	4
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Etoposide
Generic name:	Etoposide
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Ifosfamide
Generic name:	Ifosfamide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lenvatinib
Generic name:	Lenvatinib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	04-08-2020
Application type:	First submission
Review commission:	METC NedMec

Approved WMO

Date:	17-09-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-10-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	18-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-11-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	22-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-08-2022
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
EudraCT	EUCTR2019-003696-19-NL
ClinicalTrials.gov	NCT04154189
CCMO	NL72605.041.20

Study results

Date completed:	21-03-2022
Results posted:	14-03-2024

First publication
11-03-2024