A Phase II, Open Label, Randomised, Multi-centre Study to Assess the Safety and Efficacy of Agents Targeting DNA Damage Repair in Combination with Olaparib versus Olaparib Monotherapy in the Treatment of Metastatic Triple Negative Breast Cancer Patients Stratified by Alterations in Homologous Recombinant Repair (HRR)-related Genes (including BRCA1/2)

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Olaparib + AZD1775 - this treatment arm was closed.Study objectives are defined for the following patient populations:* *Breast cancer susceptible gene mutation (BRCAm)* = patients from stratum A· *Homologous Recombination Repair gene mutation (HRRm...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Breast neoplasms malignant and unspecified (incl nipple)
Study type	Interventional

Summary

ID

NL-OMON50520

Source
ToetsingOnline

Brief title
VIOLETTE

Condition

- Breast neoplasms malignant and unspecified (incl nipple)

Synonym
Breast Cancer, Homologous Recombinant Repair (HRR)-related genes

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: Ceralasertib, Homologous Recombinant Repair (HRR), Olaparib, Triple Negative Breast Cancer

Outcome measures

Primary outcome

PFS using Blinded Independent Central Review (BICR) according to Response

Evaluation Criteria in Solid Tumours (RECIST 1.1) Sensitivity analysis of PFS

using Investigator assessments according to RECIST 1.1

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Secondary outcome

These outcomes are in order of the above mentioned secondary, safety and

exploratory objectives.

SECONDARY

PFS using Blinded Independent Central Review (BICR) according to Response Evaluation Criteria in Solid Tumours (RECIST 1.1)

Sensitivity analysis of PFS using Investigator assessments according to RECIST 1.1

Objective response using BICR according to RECIST 1.1

Sensitivity analysis of objective response using Investigator assessments according to RECIST 1.1

DoR and tumour change using BICR according to RECIST 1.1

Sensitivity analysis of DoR, and tumour change using Investigator assessments according to RECIST 1.1

Time to death for any cause

PFS and objective response using BICR according to RECIST 1.1

Sensitivity analysis of PFS and objective response using Investigator assessments according to RECIST 1.1

DoR and tumour change using BICR according to RECIST 1.1

Sensitivity analysis of DoR and tumour change using Investigator assessments according to RECIST 1.1

Time to death for any cause

Mutation status of 15 genes

Minimum concentration at steady state (Cmin ss)

SAFETY

· Adverse events (AEs) (severity graded by Common Terminology Criteria for Adverse Event [CTCAE] v4)

· laboratory tests (clinical chemistry, haematology and urinalysis)

· vital signs (pulse and blood pressure [BP])

· electrocardiogram (ECG) data

· Eastern Cooperative Oncology Group performance status (ECOG PS) (see Appendix F of the protocol)

EXPLORATORY

ctDNA levels

European Organisation for research and Treatment of Cancer Quality of Life Questionnaire * Core Questionnaire (EORTC QLQ-30)-based outcome measures

May include, but is not limited to, quantified proteins, messenger ribonucleic acid (mRNA), deoxyribonucleic acid (DNA) and/or soluble circulating factors such as cytokines. Bioinformatic relationships between these markers may

additionally be assessed.

Not applicable

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Study description

Background summary

The main study is being carried out to investigate the safety and efficacy of olaparib on its own, or olaparib in combination with one novel drug (ceralasertib) in different groups of breast cancer patients. Olaparib and ceralasertib are called the study drugs. This study is *open label,* which means that both you and the Study Doctor will know which drug you are receiving.

In this study, olaparib will either be tested alone, or in combination with ceralasertib, to investigate whether the combination may increase the effectiveness of olaparib.

Drugs such as olaparib and ceralasertib, target key proteins involved in repair of deoxyribonucleic (DNA) damage, and can kill cancer cells. The Homologous Recombination Repair (HRR) proteins are involved in the repair of DNA damage. If your tumour has defects in the HRR genes may respond differently to olaparib and ceralasertib treatment.

Based on the results 3 groups of patients will be formed in this study:
A. Patients who have mutations in the breast cancer susceptible genes 1 and 2 (BRCA1/2)
B. Patients who have mutations in other genes involved in DNA repair (HRR genes)
C. Patients without any detectable HRR gene mutations

Each of these 3 groups will have approximately 116 patients. Within each subject group, patients will be assigned to one of the 2 treatment groups:
1. Olaparib alone (tablet)
2. ceralasertib (tablet) + olaparib

Study objective

Olaparib + AZD1775 - this treatment arm was closed.

Study objectives are defined for the following patient populations:
* *Breast cancer susceptible gene mutation (BRCAm)* = patients from stratum A
· *Homologous Recombination Repair gene mutation (HRRm)* = patients from stratum A and patients from stratum B
· *Non BRCAm HRRm* = patients from stratum B
· *All* = patients from any stratum
· *Non HRRm* = patients from stratum C

PRIMARY OBJECTIVE
To assess the efficacy of the combination of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy by assessment of progression free survival (PFS) in BRCAm, Non BRCAm HRRm and Non HRRm patients.

SECONDARY OBJECTIVES
To assess the efficacy of the combination of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy by assessment of PFS in HRRm and All patients.

To assess the efficacy of the of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy in terms of objective response rate (ORR)BRCAm, HRRmcombination, Non BRCAm HRRm, All and Non HRRm patients.

To assess the efficacy of the of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy in terms of
· duration of response (DoR)
· tumour change
in BRCAm, Non BRCAm HRRm and Non HRRm patients.

To assess the efficacy of the of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy in terms of overall survival (OS) in BRCAm, HRRmcombination, Non BRCAm HRRm, All and Non HRRm patients.

To compare the efficacy of the of ceralasertib+olaparib with the combination of AZD1775+olaparib in terms of
· PFS
· ORR
in BRCAm, HRRmcombination, Non BRCAm HRRm, All and Non HRRm patients.

To compare the efficacy of the combination of ceralasertib+olaparib with the combination of AZD1775+olaparib in terms of

· DoR
· tumour change
in BRCAm, Non BRCAm HRRm and Non HRRm patients.

To compare the efficacy of the combination of ceralasertib+olaparib with the combination of AZD1775+olaparib in terms of OS in BRCAm, HRRm, Non BRCAm HRRm, All and Non HRRm patients.

To explore the frequency of and describe the nature of tumour HRR (including BRCA) mutation(s) in tumour samples and to compare this with germline HRR (including BRCA) mutation status in all patients.

To assess exposure to olaparib, ceralasertib and AZD1775 in all patients in all patients.

SAFETY OBJECTIVES
To assess the safety and tolerability of the combination of ceralasertib+olaparib and the combination of AZD1775+olaparib compared with olaparib monotherapy in all patients.

EXPLORATORY OBJECTIVES
To explore the impact of study treatment on circulating tumour deoxyribonucleic acid (ctDNA) levels in all patients by exploring the relationship between ctDNA kinetics and clinical response/progression, clonal evolution of disease, predictive biomarkers of response and resistance in all patients.

To explore the effect of study treatments on patient-reported outcomes (PROs) in BRCAm, HRRm, Non BRCAm HRRm, All and Non HRRm patients.

Exploratory research into factors that may influence development of cancer and/or response to study treatment (where response is defined broadly to include efficacy, tolerability or safety) may be performed on the collected and/or stored archival biological materials which may include, but are not limited to, tumour samples, biopsies, blood and blood-derived material in all patients.

To collect and store DNA according to each country*s local and ethical procedures for future exploratory research into genes/genetic variation that may influence response (ie, distribution, safety, tolerability and efficacy) to study treatments and/or susceptibility to disease (optional) in all patients.

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Study design

Study design
This is a prospective, open label, randomised, multi-centre Phase 2 study that will assess the safety and efficacy of olaparib monotherapy versus olaparib in combination with an inhibitor of Ataxia Telangiectasia and Rad3-related protein (ATR) (ceralasertib) and olaparib monotherapy versus olaparib in combination with an inhibitor of WEE1 (AZD1775) in second or third line setting in patients with Triple Negative Breast Cancer (TNBC) stratified by qualifying tumour mutation(s) in any of 15 genes involved in the Homologous Recombination Repair (HRR) pathway.
There will be 3 treatment arms (approximately 150 patients in each treatment arm):
· Olaparib + AZD1775 - this treatment arm was closed following the ISRC meeting on the 17 Apr 2019.
· Olaparib + Ceralasertib
· Olaparib

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Intervention

The patients in this study will undergo the following:
Informed consent, sign and read.
Personal and medical history being taken.
Physical examination and vital signs
Urinalysis
Pregnancy test
Tumor assessment with CT and/or MRI scan
ECG
Questionnaire
Blood sample
Study medication intake

Study burden and risks

Risks related to study participation

Blood samples
Blood samples will be taken from a vein in your arm during the study. The taking of a blood sample may cause some discomfort and bruising, and there is a potential for infection, redness, bleeding or blood clots which may cause inflammation, swelling and pain. Other risks, although rare, include dizziness and fainting. In very rare cases it may cause nerve damage.

Risks of using an intravenous catheter
You may experience infection, pain, redness, bruising, and vein irritation from the fluid or drug being given; local swelling due to fluid accidentally

entering the tissue instead of the vein; and blood clots which may cause swelling or pain.

Electrocardiogram (ECG or heart rate)
Small sticky pads will be stuck to your chest, shoulders and hip and a machine will measure the electrical activity of your heart. We may need to clip small patches of your hair in these areas. These sticky pads may cause some local irritation, such as itching, redness, or bruising of the skin where the machine patches are placed and may be uncomfortable to remove. If the hair under the patches needs to be shaved, irritation from shaving could also occur.

Biopsy
You may experience a brief sharp pain during the procedure, bleeding if you have low platelet count (blood cells), bruising, swelling infection, or discomfort at the site of the biopsy. These are generally easily managed, but can be more serious and require admission to hospital. The location where the tumour sample is taken may require stitches which will be removed by a study nurse or Study Doctor about 1 week after the biopsy. The biopsy site should be kept covered, clean, and dry until it heals. Optional tumour tissue biopsies will be obtained only on progression.

Computed tomography (CT) scan
If you have a CT scan you will be exposed to a limited and medically acceptable dose of radiation. The amount of radiation you are exposed to during a CT scan varies; depending on how much of your body is scanned. There is always a slight risk of damage from being exposed to any radiation. It is thought that exposure to radiation during CT scans could slightly increase your chances of developing cancer many years later, although this risk is thought to be very small. Please talk to the Study Doctor about the amount of radiation from these scans.
You may feel some discomfort or anxiety when lying inside of the CT scanner. Before the scan, contrast medium may be injected into one of your veins; this is like a dye and will spread through your body and will help give clearer images. The injection of contrast medium may cause some discomfort and bruising. Some people can have allergic reactions to the dye put in their veins for these tests. The dye (contrast medium) that is injected into your body may cause you to get a metallic taste in your mouth, to feel warm, and cause nausea and vomiting. In addition, the dye may cause an allergic reaction that could be mild to serious, and could be life threatening. The allergic reactions can cause itching or rash. More serious allergic reactions can cause difficulty breathing, dangerously low blood pressure, or kidney damage. If you know that you have had an allergic reaction to an intravenous dye in the past, please tell the study staff.

Magnetic Resonance Imaging (MRI) scan:
A MRI scan is painless and will not expose you to X-ray radiation. This process is safe for most people. Subjects with metal near important organs may not receive an MRI. The metal may be drawn away from the body and towards the large

magnet, which could cause injury. Talk to the Study Doctor if you have metal in your body or if you are uncomfortable in small spaces. Before these scans, a contrast medium may be injected into one of your veins. A contrast medium is like a dye that will spread through your body and will help give clearer images. The injection of contrast medium may cause some discomfort and bruising. There is a risk of possible serious allergic reactions in some people who receive contrast medium. Some people with kidney disease may have a severe reaction of skin thickening, joint pain and/or swelling, and, in rare cases, lung and heart problems and even death. Some people may feel frightened by the cramped space inside the machine or by the loud, repeated sounds the machine makes. The greatest risk of having an MRI is the chance of metal objects flying through the air toward the magnet and hitting you. To reduce this risk, all people giving and getting the MRI scan will be asked to remove all metal from their clothing and all metal objects from their pockets. Please inform the Study Doctor if you have metal in your body from an operation, since you may not be able to have a MRI scan. Also, if you have a pacemaker you should not have a MRI scan.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Protocol V2.0 section 3.1
At Screening Part 1, prior to HRR mutation testing being carried out, the criteria marked with an asterisk (*) must be fulfilled by the patients who do not have a known BRCAm status and are being considered for this study. , 1. * Provision of informed consent prior to any study specific procedures
2. * Patients must be male or female *18 years of age
3. * Progressive cancer at the time of study entry
4. * Histologically or cytologically confirmed TNBC with evidence of metastatic disease (defined as ER and PgR negative [IHC nuclear staining <1% positive] and HER2 negative [IHC 0, 1+ or IHC 2+ with corresponding ISH non-amplified of ratio less than 2.0 or ISH non-amplified ratio less than 2.0] as per ASCO-CAP HER2 guideline recommendations 2013
5. * Patients must have received at least 1 and no more than 2 prior lines of treatment for metastatic disease with an anthracycline (eg, doxorubicin, epirubicin) and/or a taxane (eg, paclitaxel, docetaxel) unless contraindicated, in either the neo-adjuvant, adjuvant or metastatic setting..
* Patients who have received platinum (cisplatin or carboplatin, either as monotherapy or in combination) for advanced breast cancer are eligible to enter the study provided there has been no evidence of disease progression during the platinum chemotherapy.
* Patients who have received prior platinum based chemotherapy are eligible if platinum was given either as potentially curative treatment for a prior non breast cancer (eg, ovarian cancer) with no evidence of disease for *5 years prior to study entry or as adjuvant/neoadjuvant treatment for breast cancer provided at least 12 months have elapsed between the last dose of platinum-based treatment and randomisation
6. Confirmed presence of qualifying HRR mutation or absence of any HRR mutation in tumour tissue by the Lynparza HRR assay.
7. *At least one measurable lesion that can be accurately assessed at baseline by computed tomography (CT) (magnetic resonance imaging [MRI] where CT is contraindicated) and is suitable for repeated assessment as per RECIST 1.1.
8. Patients must have normal organ and bone marrow function measured within 28 days prior to randomisation as defined below:
(a) Haemoglobin (Hb) ?10.0 g/dL with no blood transfusions (packed red blood cells) in the past 28 days
(b) Absolute neutrophil count (ANC) ? 1.5 x 109/L
(c) Platelet count ?100 x 109/L with no platelet transfusions in the past 28

days
(d) Total bilirubin *1.5 x institutional upper limit of normal (ULN) unless the patient has documented Gilbert*s Syndrome
(e) Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) *2.5 x institutional ULN unless liver metastases are present in which case they must be *5 x ULN
(f) Patients must have creatinine clearance (CrCl) estimated using the Cockcroft-Gault equation of ?51 mL/min:
Estimated CrCl <= (140-age [years]) x weight (kg) (x F)a serum creatinine (mg/dL) x 72
a where F<=0.85 for females and F<=1 for males
9. * ECOG PS 0-1 within 28 days of randomisation.
10. * Postmenopausal or evidence of non childbearing status for women of childbearing potential: negative urine or serum pregnancy test within 28 days of study treatment and confirmed prior to treatment on Day 1.
11. Women of childbearing potential and their partners, who are sexually active, must agree to the use of 2 highly effective forms of contraception in combination (as described in Appendix E) from the signing of the informed consent, throughout the period of taking study treatment and for at least 1 month after last dose of study drug(s), or they must totally/truly abstain from any form of sexual intercourse (as described in Appendix E).
12. Male patients must use a condom during treatment and for 6 months after the last dose of study drug(s) when having sexual intercourse with a pregnant woman or with a woman of childbearing potential. Female partners of male patients should also use a highly effective form of contraception (see Appendix E for acceptable methods) for 6 months after the last dose of study drug(s) if they are of childbearing potential.
13. Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations.
14. * Patients must have a life expectancy of *16 weeks.

Exclusion criteria

Protocol V2.0 section 3.2
Patients should not enter the study if any of the following exclusion criteria are fulfilled:
1. * Involvement in the planning and/or conduct of the study (applies to AstraZeneca staff and/or staff at the study site).
2. Cytotoxic chemotherapy, hormonal or non hormonal targeted therapy within 21 days of Cycle 1 Day 1 is not permitted. Palliative radiotherapy must have been completed 21 or more days before Cycle 1 Day 1. The patient can receive a stable dose of bisphosphonates or denosumab for bone metastases, before and during the study as long as these were started at least 5 days prior to study treatment.
3. * More than 2 prior lines of cytotoxic chemotherapy for metastatic disease.

- Prior treatments with hormonal therapy and non hormonal targeted therapy are allowed and not counted as a prior line of cytotoxic chemotherapy.
- For the purposes of this protocol, the combination of an aromatase inhibitor and everolimus is not considered cytotoxic chemotherapy.
- Treatment with biologics will not be considered as prior line of therapy.
4. * Previous randomisation in the present study.
5. * Previous treatment with a PARP inhibitor (including olaparib) or other DDR inhibitor (unless treatment was for less than 3 weeks duration and at least 12 months have elapsed between the last dose and randomisation. Patients that did not tolerate prior treatment are excluded).
6. * Exposure to a small molecule IP within 30 days or 5 half-lives (whichever is longer) prior to randomisation. The minimum washout period for immunotherapy shall be 42 days.
7. * Patients with MDS/AML or with features suggestive of MDS/AML.
8. * Patients with second primary cancer, EXCEPTIONS: adequately treated non melanoma skin cancer, curatively treated in-situ cancer of the cervix, Ductal Carcinoma in Situ (DCIS), stage 1 grade 1 endometrial carcinoma, or other solid tumours curatively treated with no evidence of disease for * 5 years prior to study entry (including lymphomas [without bone marrow involvement]).
9. Mean resting corrected QTc interval using the Fridericia formula (QTcF) >470 msec/female patients and >450 msec for male patients (as calculated per institutional standards) obtained from 3 ECGs performed 2-5 minutes apart at study entry, or congenital long QT syndrome.
No longer applicable from CSP V6.0 - AZD1775 should not be given to patients who have a history of Torsades de pointes unless all risk factors that contributed to Torsades have been corrected. AZD1775 has not been studied in patients with ventricular arrhythmias or recent myocardial infarction.
10. Any of the following cardiac diseases currently or within the last 6 months defined by New York Heart Association (NYHA) * Class 2:
- Unstable angina pectoris
- Congestive heart failure
- Acute myocardial infarction
- Conduction abnormality not controlled with pacemaker or medication
- Significant ventricular or supraventricular arrhythmias (patients with chronic rate-controlled atrial fibrillation in the absence of other cardiac abnormalities are eligible)
11. Concomitant use of known strong cytochrome P (CYP) 3A inhibitors (eg. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir) or moderate CYP3A inhibitors (eg. ciprofloxacin, erythromycin, diltiazem, fluconazole, verapamil). The required washout period prior to starting study treatment is 2 weeks.
No longer applicable from CSPv7.0: Patient has had prescription or non-prescription drugs or other products known to be sensitive CYP3A4 substrates or CYP3A4 substrates with a narrow therapeutic index, or to be moderate to strong inhibitors/inducers of CYP3A4 which cannot be discontinued 2 weeks prior to Day 1 of dosing and withheld throughout the study until 2 weeks

after the last dose of study drug (see Appendix H).
No longer applicable from CSPv7.0: Transporter studies (in vitro) have shown that AZD1775 is an inhibitor of breast cancer resistance protein (BCRP). Please refer to Appendix H for use with BCRP substrates.
No longer applicable from CSPv7.0: Patients should stop using herbal medications 7 days prior to first dose of study treatment. Please see Appendix H for further details.
12. Concomitant use of known strong (eg. phenobarbital, enzalutamide, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John*s Wort) or moderate CYP3A inducers (eg. bosentan, efavirenz, modafinil). The required washout period prior to starting study treatment is 5 weeks for enzalutamide or phenobarbital and 3 weeks for other agents.
13. Persistent toxicities (* CTCAE grade 2) caused by previous cancer therapy, excluding alopecia and CTCAE grade 2 peripheral neuropathy.
14. Major surgery within 2 weeks of starting study treatment: patients must have recovered from any effects of any major surgery.
15. * Immunocompromised patients, eg, patients who are known to be serologically positive for human immunodeficiency virus (HIV).
16. * Patients with known active hepatitis (ie, hepatitis B or C).
17. * Patients considered a poor medical risk due to a serious, uncontrolled medical disorder, non malignant systemic disease or active, uncontrolled infection.
* Examples include, but are not limited to, uncontrolled ventricular arrhythmia, recent (within 3 months) myocardial infarction, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, extensive interstitial bilateral lung disease on High Resolution CT scan or any psychiatric disorder that prohibits obtaining informed consent, and any other medical condition that, in the opinion of the Investigator, places the patient at unacceptable risk of toxicity.
18. * Patients with symptomatic uncontrolled brain metastases.
- A scan to confirm the absence of brain metastases is not required. Patients with spinal cord compression unless considered to have received definitive treatment for this and evidence of clinically stable disease (SD) for 28 days.
- * Patients with a history of treated central nervous system (CNS) metastases are eligible, provided they meet all of the following criteria: Disease outside the CNS is present. No clinical evidence of progression since completion of CNS-directed therapy. Minimum of 3 weeks between completion of radiotherapy and Cycle 1 Day 1 and recovery from significant (Grade *3) acute toxicity with no ongoing requirement for >10 mg of prednisone per day or an equivalent dose of other corticosteroid. If on corticosteroids, the patient should be receiving a stable dose of corticosteroids, started at least 4 weeks prior to treatment.
19. * Patients unable to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the study medication.
20. * Patients with a known hypersensitivity to olaparib, AZD1775, ceralasertib, or any of the excipients of the products.

21. Pregnant or breast feeding women.

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:	Recruitment stopped
Start date (anticipated):	16-04-2019
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AZD6738
Generic name:	Ceralasertib
Product type:	Medicine
Brand name:	Lynparza
Generic name:	Olaparib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	20-02-2018

Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-11-2018
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-01-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	13-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-02-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-05-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-07-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	06-08-2019

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	19-12-2019
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-01-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-01-2020
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Review commission:	METC Brabant (Tilburg)
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Approved WMO Date:	27-07-2020
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Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-11-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	EUCTR2017-002361-22-NL
ClinicalTrials.gov	NCT03330847
CCMO	NL63865.028.18

Study results

Date completed:	24-09-2020
Actual enrolment:	3