A Randomized, Double-Blind, Placebo-Controlled, Phase IIIb Study of the Efficacy and Safety of Continuing Enzalutamide in Chemotherapy Naïve Metastatic Castration Resistant Prostate Cancer Patients Treated with Docetaxel plus Prednisolone Who Have Progressed on Enzalutamide Alone.

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The primary objective of this research is to compare the efficacy of continuing treatment with enzalutamide after adding docetaxel and prednisolone versus placebo plus docetaxel and prednisolone, as measured by progression-free survival (PFS) in...

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

Summary

ID

NL-OMON47746

Source
ToetsingOnline

Brief title
PRESIDE

Condition

- Metastases
- Prostatic disorders (excl infections and inflammations)

Synonym
Malignancy of the prostate with metastases no longer sensitive for the castration treatment, Metastatic malignant prostate tumor resistant for the castration treatment.

Research involving
Human

Sponsors and support

Primary sponsor: Astellas Pharma
Source(s) of monetary or material Support: Astellas Pharma Europe Ltd

Intervention

Keyword: Chemotherapy naïve metastatic Castration Resistant Prostate Cancer , Continued Enzalutamide, Docetaxel, Efficacy and safety

Outcome measures

Primary outcome

The primary efficacy endpoint is PFS with progression defined as radiographic

progression, unequivocal clinical progression, or death on study. PFS is

defined as the time from randomization to the earliest objective evidence of

radiographic progression, unequivocal clinical progression, or death on study,

whichever occurs first.

• Radiographic disease progression is defined for bone disease by the

appearance of 2 or more new lesions on whole-body radionuclide bone scan per

PCWG2 criteria or for soft tissue disease by RECIST 1.1;

• Unequivocal clinical progression is defined as any of the following:

o new onset cancer pain requiring chronic administration of opiate

analgesia;

o deterioration from prostate cancer of ECOG performance status score to 3

or higher;

o initiation of subsequent lines of cytotoxic chemotherapy or radiation therapy or surgical intervention due to complications of tumor progression. Radiotherapy for palliative management of symptoms due to prostate cancer will not be considered unequivocal clinical progression;

• Death on study is defined as death within 112 days of treatment discontinuation without objective evidence of radiographic progression.

Secondary outcome

Secondary endpoints include:

• Time to PSA progression, defined as the time from randomization to the date of the first PSA value in Period 2 demonstrating progression (Period 2). The PSA progression date is defined as the date that a >= 25% increase and an absolute increase of >= 2 ng/mL above the nadir recorded in Period 2 is documented, which must be confirmed by a second consecutive value obtained at least 3 weeks later;

• PSA response, defined as the percentage change in PSA from randomization to Week 13 (or earlier for those that discontinue therapy), as well as the maximum decline in PSA that occurs at any point after treatment;

• Objective response rate, defined as the best overall radiographic response after randomization as per Investigator assessments of response for soft tissue disease per RECIST 1.1, in subjects who have a measurable tumor;

• Time to pain progression, defined as the time to an increase of >= 30% from randomization in the mean of BPI-SF pain intensity item scores (items 3, 4, 5, and 6);

• Time to opiate use for cancer-related pain, defined as the time to initiation of chronic administration of opiate analgesia;

• Time to first SRE, defined as the time from randomization to radiation therapy or surgery to bone, pathologic bone fracture, spinal cord compression, or change of antineoplastic therapy to treat bone pain;

• Quality of life, as assessed using FACT-P and EQ-5D-5L.

Other Endpoints:

• Cumulative dose of docetaxel.

• Health resource use (hospitalization and duration thereof; number and types of visits to a health professional) in Period 1 and Period 2

Exploratory Endpoints:

• To analyze candidate biomarkers in circulation for association with response or progression and for identifying mechanisms of resistance.

Safety Endpoints:

• Safety in both Periods will be assessed by AEs, clinically significant changes in physical examination, vital signs, laboratory values, and ECGs.

• Deaths, defined as deaths due to any cause, will be summarized descriptively.

Study description

Background summary

When patients progress on enzalutamide alone a treatment of docetaxel and prednisolone can be initiated. At this moment this combination therapy is

standard in the Netherlands.
There is, however, no insight yet in the best treatment options when patients progress on enzalutamide. Studies are needed to define if continued enzalutamide treatment beyond progression combined with docetaxel and prednisolon is effective for the treatment of progressive mCRPC. After initial response on enzalutamide, progression of the disease can occur due to resistance of the prostate cancer. However, it is expected that beside resistant cells there are also cells that are still hormone-sensitive. In this study it will be investigated if continues use of enzalutamide has an effect while standard chemotherapy treatment is started. This study aims at the efficacy of continuing enzalutamide in the treatment of progressive metastasized castration resistant prostate cancer with docetaxel and prednisolone.

Study objective

The primary objective of this research is to compare the efficacy of continuing treatment with enzalutamide after adding docetaxel and prednisolone versus placebo plus docetaxel and prednisolone, as measured by progression-free survival (PFS) in subjects with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) with progression during treatment with enzalutamide alone.

The secondary objective is to evaluate the effect of continuing treatment with enzalutamide after adding docetaxel and prednisolone versus placebo plus docetaxel and prednisolone, as measured by the following endpoints in subjects with chemotherapy-naïve metastatic castration-resistant prostate cancer (mCRPC) with progression during treatment with enzalutamide alone:
• Time to prostate-specific antigen (PSA) progression;
• PSA response;
• Objective response rate;
• Time to pain progression;
• Time to opiate use for cancer-related pain;
• Time to first skeletal-related event;
• Quality of life.

Safety profile including cumulative dose of docetaxel and Health Resource Use will be described for
these subjects.

Study design

This double-blind, randomized, placebo-controlled trial of patients with chemotherapy- naïve mCRPC will evaluate the efficacy and safety of continuing treatment with enzalutamide plus docetaxel and prednisolone compared with treatment with placebo in combination with docetaxel and prednisolone. The

study will be conducted in consecutive periods of open label treatment with enzalutamide followed by randomized double-blind treatment with continued enzalutamide or placebo in combination with docetaxel and prednisolone.

Open Label (Period 1):
Subjects will attend a Screening Visit to determine eligibility for open label treatment in Period 1.
Following Screening, enrolled subjects will receive open label treatment with enzalutamide (160 mg/day). At Week 13, all subjects will be assessed by PSA and imaging. The initial PSA response (stable or declining) must be confirmed by a second consecutive value at least 3 weeks later. As PSA may not remain stable or decline in all subjects who subsequently benefit from enzalutamide, this study design is based on the hypothesis that subsequent addition of docetaxel will be of greater benefit in those subjects who have a confirmed initial PSA response. Therefore, subjects with no confirmed PSA response or evidence of radiographic progression (assessed at Week 13) will be ineligible for participation in Period 2 and will typically have safety follow up; however, Period 1treatment may continue for some subjects as long as the investigator considers it to be of clinical benefit (stopping on initiation of any new antineoplastic therapy). Subjects with confirmed PSA response will continue Period 1 until disease progression as supported by evidence of at least one of the following criteria (see Assessments):
• PSA progression with rapid PSA doubling time (PSA-DT) defined as:
o PSA rise of >= 25% and an absolute increase of >= 2 ng/mL above nadir, confirmed by a second PSA value at least 3 weeks later, and
o PSA-DT of <= 12 weeks determined in at least 3 PSA measurements collected at intervals of 4 or more weeks apart during a period of 3 or more months;
• Radiographic progression defined as:
o Bone disease progression, or;
o Soft tissue disease progression.
Administration of open label enzalutamide will continue until randomization to Period 2 treatment, confirmation of ineligibility for Period 2 treatment (subjects will be discontinued from the study), intolerable toxicity, subject withdrawal, or death, whichever occurs first.

Randomization (Period 2):
Subjects with confirmed disease progression on enzalutamide alone who continue to meet all eligibility criteria may proceed to randomization. Randomization must occur within 4 weeks of progression observed in Period 1.
Treatment allocation will be in a 1:1 ratio, stratified by disease progression (evidence of radiographic progression or not) in Period 1 to the following treatments:
• Enzalutamide (160 mg daily) in combination with docetaxel (75 mg/m2 every 3 weeks) and prednisolone (10 mg daily);
• Enzalutamide placebo (daily) in combination with docetaxel (75 mg/m2 every 3 weeks) and prednisolone (10 mg daily).
Administration of docetaxel will continue for up to 10 cycles, however subjects

assessed by the Investigator to be benefiting from treatment may continue on docetaxel for additional cycles. Subjects who discontinue docetaxel before completion of 10 cycles (e.g. for toxicity) may continue treatment with IMP and will continue to attend study visits (at 12 weekly intervals) for assessments until IMP discontinuation criteria or endpoint criteria are met.
Administration of blinded enzalutamide/placebo will continue until disease progression, intolerable toxicity, subject withdrawal or death, whichever occurs first.

Follow-up:
All subjects will have a safety follow-up visit 30 days after the last dose of Investigational Medicinal Product (IMP) or prior to the initiation of a subsequent antineoplastic therapy for prostate cancer, whichever occurs first.
In Period 2, subjects who discontinue IMP for a reason other than disease progression will continue to attend follow-up visits (at 12 weekly intervals) for assessments until withdrawal of consent, disease progression or death.

Biomarker Sub-Study:
Subjects in a subset of countries and sites will be invited to participate in a voluntary, exploratory, biomarker sub-study. For subjects who have consented to provide samples for this sub-study, blood samples for circulating biomarker analysis will be taken at the following timepoints:
- Period 1: Week 1/Day1 (pre dosing with enzalutamide), Week 5, Week 13, and when subjects progress clinically (4 samples).
- Period 2: Week 1/Day 1 (pre study drug in Period 2), Cycle 2 (Week 4), Cycle 5 (Week 13), Cycle 9 (Week 25), when subjects progress clinically or reach another endpoint in the study and at Follow-Up (30 days after last dose of IMP) (6 samples)
Any subject who consents to participate in the biomarker sub-study, but fails to provide a valid baseline sample for Period 1, may still participate in Period 2 of the biomarker sub-study. In this case, the last sample of Period 1 (the sample taken when they progress clinically) should be taken as part of the baseline for Period 2. Informed Consent for the biomarker samples must be taken before any samples are collected. Samples are to be handled according to the laboratory manual, and shipped to a central laboratory for processing.

Extension Period:
When sufficient numbers of subjects have been randomized into Period 2 (around 274), enrollment to Period 2 will close. Subjects who are still in Period 1 will have the opportunity to continue open label enzalutamide via an Extension Period until the investigator or subject decides it is no longer in the subject*s best interests to continue; a decision to initiate alternative antineoplastic therapy is made; or
there is disease progression, intolerable toxicity, subject withdrawal or death, whichever occurs first. Assessments will be limited to collection of efficacy and laboratory assessments that are performed as part of standard of care for the subject, Serious Adverse Events (SAEs) and Adverse Events (AEs).

Protocol-specified efficacy and laboratory assessments will cease.
Similarly, when at least 182 endpoint-events have occurred in Period 2 of the study, the data will be cleaned and analyzed. Allowing for attrition, there may be some subjects still active in Period 2 when this data analysis cut-off is reached. These subjects will be able to continue to receive blinded study drug until the study is unblinded after database lock, at which time subjects will then be able to
continue receiving the most efficacious treatment (docetaxel + enzalutamide OR docetaxel only) until the investigator or subject decides it is no longer in the subject*s best interests to continue study drug; a decision to initiate alternative antineoplastic therapy is made; or there is disease progression, intolerable toxicity, subject withdrawal or death, whichever occurs first. Assessments will be limited as described above. Assuming a subject is still taking blinded study drug when the results of the study are known, subjects will be given the opportunity to switch to the drug combination shown to be the most effective.

Intervention

In period 1 all subjects will receive open-label enzalutamide 160 mg once daily (4 x 40 mg capsules) oral, with or without food, until randomisation to period 2 treatment, confirmation of ineligibility for period 2 treatment, intolerable toxicity, patient withdrawal, or death.
After the open-label period the subjects that will continue to period 2 will be randomized to double-blind treatment in a 1:1 randomisation ratio:
- Arm 1: docetaxel (75 mg/m2/3 weeks), prednisolone (or prednisone as substitute) 10 mg/day (2 x 5 mg tablet), enzalutamide 160 mg (4 x 40 mg capsules) once daily, oral with or without food;
- Arm 2: docetaxel (75 mg/m2/3 weeks), prednisolon 10 mg/day (2 x 5 mg tablet), placebo capsules (4 capsules) once daily, oral with or without food.
Docetaxel will be administered every 3 weeks over 1 hour by an intravenous infusion. Prednisolone/prednisone will be administered as 1 tablet (5 mg) by mouth twice daily with food.

Study burden and risks

An estimation of the burden and risks are reflected in previous paragraphs. The risks of participation include adverse reactions of the study medications and the risks of the study procedures and tests are listen in paragraph E9 and E9a. See paragraph E2 for the estimated burden.

For subjects who consent to provide samples for biomarker analysis, an addition of no more than approximately 300ml of blood will be taken, in addition to the amounts specified above for the main study.

Contacts

Public
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Scientific
Astellas Pharma

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion/Exclusion Criteria:
Inclusion:
Inclusion Criteria - Period 1 (assessed at the Screening Visit)
Subjects must meet the following criteria prior to initiation of IMP:
1. Age 18 or older;
2. Independent Ethics Committee (IEC)-approved written Informed Consent and privacy language
as per national regulations must be obtained from the subject or legally authorized representative
prior to any study-related procedures (including withdrawal of prohibited medication, if applicable);
3. Histologically confirmed adenocarcinoma of the prostate without neuroendocrine

differentiation
or small cell features;
4. Ongoing ADT with a luteinizing hormone-releasing hormone (LHRH) agonist or antagonist at a
stable dose and schedule within 4 weeks of initiation of IMP, or bilateral orchiectomy (i.e., surgical or medical castration);
5. Serum testosterone level <= 1.73 nmol/L (<= 50 ng/dL);
6. Metastatic (M1) disease documented by at least 2 bone lesions on bone scan, or soft tissue disease documented by CT/MRI;
7. Progressive disease at study entry defined as the following occurring in the setting of castrate
levels of testosterone:
• PSA progression defined by a minimum of three rising PSA levels with an interval of >= 1 week between each determination.
• The PSA value at Screening should be >= 2 µg/L (>= 2 ng/mL). In the event of prior androgen
receptor inhibitor use, the most recent local PSA and the Screening PSA assessed by the central laboratory (central PSA) must be obtained at least 4 weeks after the last dose of androgen receptor inhibitor;
8. Asymptomatic or minimally symptomatic prostate cancer (BPI-SF question 3 score of < 4) at
Screening;
9. ECOG performance score of 0-1 at Screening;
10. Estimated life expectancy of >= 12 months from Screening;
11. Be suitable and willing to receive chemotherapy as part of the trial;
12. Able to swallow the IMP and comply with study requirements;
13. Subjects and their female spouse/partners who are of childbearing potential must be using highly effective contraception consisting of 2 forms of birth control* (one of which must be a condom) starting at Screening and continue throughout the study period and for 3 months after the final IMP administration;
14. Subjects must not donate sperm starting at Screening and throughout the study period and for 3 months after the final IMP administration. A condom is required throughout the study period
and for 3 months after the final IMP administration if the subject is engaged in sexual activity with a pregnant woman;
15. Subject agrees not to participate in another interventional study while on treatment. Subjects who are participating in a control arm of an interventional study which includes only standard of care, or in an observational phase following an interventional study, may be eligible for this study, providing they meet all the other entry criteria.;Inclusion Criteria - Period 2 (assessed at the Period 2 Eligibility Assessment)
Subjects must meet the following criteria prior to randomization:
1. Have confirmed progressive disease on open label enzalutamide treatment, defined as one or
more of:
• PSA progression with rapid PSA-DT defined as a PSA rise of >= 25% and an absolute increase of >= 2 ng/mL above nadir, confirmed by a second PSA value at least 3 weeks later and a PSA-DT of <= 12 weeks determined in at least 3 PSA measurements collected at

intervals of 4 or more weeks apart during a period of 3 or more months;
• Bone disease progression defined by the appearance of 2 or more new bone lesions on whole-body radionuclide bone scan per the PCWG2 criteria;
• Soft tissue disease progression per the RECIST 1.1, with a consistent methodology applied to assess any given subject;
2. Ongoing ADT with a LHRH agonist or antagonist at a stable dose and schedule for at least 4 weeks, or bilateral orchiectomy (i.e., surgical or medical castration);
3. Serum testosterone level <= 1.73 nmol/L (<= 50 ng/dL);
4. ECOG performance score of 0-2;
5. Subjects receiving bisphosphonates or denosumab for bone health must have been on a stable
dose for at least 4 weeks;
6. Able to swallow the IMP and comply with study requirements;
7. Subjects and their female spouse/partners who are of childbearing potential must be using highly effective contraception consisting of 2 forms of birth control* (one of which must be a condom) starting at Screening and continue throughout the study period and for the later of 3 months after the final IMP administration or 6 months after the final docetaxel administration;
8. Subjects must not donate sperm starting at Screening and throughout the study period and for the later of 3 months after the final IMP administration or 6 months after the final docetaxel
administration. A condom is required throughout the study period and for 3 months after the final IMP administration if the subject is engaged in sexual activity with a pregnant woman;
9. Be suitable and willing to receive chemotherapy as part of the trial.
*Acceptable forms of birth control include:
• Established use of oral, injected or implanted hormonal methods of contraception.
• Placement of an intrauterine device (IUD) or intrauterine system (IUS).
• Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository.

Exclusion criteria

Exclusion Criteria - Period 1 (assessed at the Screening Visit)
Subject will be excluded from participation if any of the following apply:
1. Absolute neutrophil count (ANC) < 1,500/µL, platelet count < 100,000/µL, or hemoglobin < 6.2 mmol/L (< 10 g/dL)
(NOTE: subjects must not have received any growth factors or blood transfusions within seven
days prior to the hematologic laboratory values obtained at Screening);
2. Total bilirubin > upper limit of normal (ULN); alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >= 2.5 times ULN; Child-Pugh B and C hepatic impairment;
3. Creatinine > 177 µmol/L (> 2 mg/dL);
4. Albumin <= 30 g/L (<= 3.0 g/dL;
5. Prior treatment with the following agents for the treatment of prostate cancer:
• Aminoglutethimide;

• Ketoconazole;
• Abiraterone;
• Enzalutamide or participation in a clinical trial of enzalutamide;
• 223Ra, 89Sr, 153Sm, 186Re/188Re;
• Immunomodulatory therapies (e.g. Sipuleucel-T, DCVAC);
• Cytotoxic chemotherapy (e.g. docetaxel, cabazitaxel, mitoxantrone, estramustine);
• Participation in a clinical trial of an investigational agent that inhibits the androgen receptor or androgen synthesis (e.g. ARN-509, ODM-201, VT-464; unless the treatment was placebo);
6. Current or prior treatment within 4 weeks prior to initiation of IMP with the following agents for
the treatment of prostate cancer:
• Antiandrogens (e.g., bicalutamide, nilutamide, flutamide);
• 5-α reductase inhibitors (e.g., finasteride, dutasteride);
• Estrogens;
• Anabolic steroids;
• Drugs with antiandrogenic properties such as spironolactone > 50 mg/kg;
• Progestational agents;
7. Subject has received investigational therapy within 28 days or 5 half-lives, whichever is longer,
prior to initiation of IMP;
8. Use of opiate analgesia for pain from prostate cancer within 4 weeks prior to initiation of IMP;
9. Radiation therapy to bone lesions or prostatic bed within 4 weeks prior to initiation of IMP;
10. Major surgery within 4 weeks prior to initiation of IMP;
11. History of seizure or any condition that may predispose to seizures at any time in the past (e.g.,
prior cortical stroke, brain arteriovenous malformation, head trauma with loss of consciousness
requiring hospitalization). History of loss of consciousness or transient ischemic attack within 12
months prior to Screening;
12. Known or suspected brain metastasis or active leptomeningeal disease;
13. History of another malignancy within the previous 5 years other than non-melanoma skin cancer;
14. Clinically significant cardiovascular disease including:
• Myocardial infarction within six months prior to Screening;
• Uncontrolled angina within three months prior to Screening;
• Congestive heart failure New York Heart Association (NYHA) class 3 or 4, or subjects with history of congestive heart failure NYHA class 3 or 4 in the past, unless a screening echocardiogram or multi-gated acquisition scan (MUGA) performed within 3 months results in a left ventricular ejection fraction that is >= 45%;
• History of clinically significant ventricular arrhythmias (e.g., ventricular tachycardia, ventricular fibrillation, torsades de pointes);
• History of Mobitz II second degree or third degree heart block without a permanent pacemaker in place;
• Bradycardia as indicated by a heart rate < 45 beats per minute on the screening ECG or

physical examination;
• Uncontrolled hypertension as indicated by a resting systolic blood pressure > 170 mmHg or diastolic blood pressure > 105 mmHg at Screening;
15. Gastrointestinal disorders affecting absorption (e.g., extensive small bowel resection, active
inflammatory bowel disease);
16. Medical contraindications to the use of prednisolone or docetaxel;
17. Allergies to any of the active ingredients or excipients in the study drugs;
18. Any condition which, in the Investigator*s opinion, makes the subject unsuitable for study participation.
Exclusion Criteria - Period 2 (assessed at the Period 2 Eligibility Assessment)
Subject will be excluded from participation if any of the following apply:
1. Cancer pain requiring chronic administration of opiate analgesia (parenteral opiate use for >=7
days or use of WHO Analgesic Ladder Level 3 oral opiates for >=3 weeks;
2. ANC < 1,500/µL, platelet count < 100,000/µL, or hemoglobin < 6.2 mmol/L (< 10 g/dL) (NOTE: subjects must not have received any growth factors or blood transfusions within seven
days prior to the hematologic laboratory values obtained at the Period 2 Eligibility Assessment);
3. Total bilirubin > ULN; ALT or AST >= 2.5 times ULN; Child-Pugh B and C hepatic impairment;
4. Creatinine > 177 µmol/L (> 2 mg/dL);
5. Albumin <= 30 g/L (<= 3.0 g/dL).

Study design

Design

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

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	01-12-2014
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Docetaxel
Generic name:	Docetaxel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Xtandi
Generic name:	Enzalutamide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	02-06-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-06-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	21-08-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-09-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-08-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-09-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-12-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-01-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-12-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-01-2019
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-05-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-06-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-08-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-08-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-09-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO

Date:	04-04-2021
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Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-04-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-09-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-09-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-05-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-05-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

(Nieuwegein)

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	EUCTR2013-004711-50-NL
ClinicalTrials.gov	NCT02288247
CCMO	NL49804.100.14