Parallel-Group, Placebo-Controlled Randomized Study Investigating the Effect of Intravenous Iso-osmolar Iodinated Contrast Material Iodixanol (Visipaque* Injection 320 mgI/mL) on Renal Function in Adults with Chronic Kidney Disease (CKD) Stage III or Stage IV Who Have Undergone Endovascular Aneurysm Repair (EVAR)

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Primary Objective:* To demonstrate the safety of intravenous (i.v.) iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in contrast-enhanced computed tomography (CECT) for CKD stage III/IV patients by evaluating the incidence of...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON46580

Source
ToetsingOnline

Brief title
VI-CKD Study

Condition

- Nephropathies

Synonym
use of contrastfluid in CKD

Research involving
Human

Sponsors and support

Primary sponsor: GE Healthcare Ltd. and its Affiliates
Source(s) of monetary or material Support: sponsor

Intervention

Keyword: Chronic Kidney Disease, Endovascular Aneurysm Repair, Visipaque

Outcome measures

Primary outcome

The primary outcome measure in this study will be the incidence of AKI stage *1

(in accordance with AKIN SCr criteria ([AKIN 2015] [Mehta et al. 2007])

Secondary outcome

Secondary outcome measures will include:

* Assessing the incidence of AKI stage *2 (in accordance with AKIN SCr

criteria).

* Assessing the incidence of AKI by other definitions (standard definition of

CIN [Mehran and Nikolsky 2006] and AKI stages *2 by Waikar criteria [Waikar and

Bonventre 2009]).

* Assessing the incidence of AKI related morbidity and mortality at 6 months

(Follow-Up 3). This will be assessed by an independent Critical Events

Adjudication Committee (CEAC). The independent CEAC will be appointed at the

commencement of the study before any patients are enrolled.

* Assessment of image quality/diagnostic confidence. Exploratory outcome

measures will include:

* Changes in SCr, cystatin C, N-GAL, and NephroCheck® biomarkers from baseline

up to 48 hours post

contrast/saline infusion.

* Determination of GFR as measured by an ORFM in a subset of patients.

Study description

Background summary

Contrast materials are liquids and some types are injected directly into the blood before having an X-ray or computerised tomography (CT) scan. Contrast materials improve X-ray or CT scan images helping doctors see the area of the body under investigation more clearly. This helps them to understand how best to treat you. Patients who have undergone an EVAR procedure need to have regular check-ups, usually with CT scans. In this study, we are looking at a contrast material called Visipaque which is approved for use in 100 countries and has been used in CT scans for over 20 years. Often, patients who have chronic kidney disease (CKD) do not receive contrast materials because doctors are concerned that this may increase the risk of damage to the kidney. The doctors are looking for the best way to observe and treat patients with your medical condition and therefor it is needed to know if the use of contrast fluids is having a negative impact on the renal functioning.

Study objective

Primary Objective:
* To demonstrate the safety of intravenous (i.v.) iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in contrast-enhanced computed tomography (CECT) for CKD stage III/IV patients by evaluating the incidence of acute kidney injury (AKI) stage *1, per acute kidney injury network (AKIN) serum creatinine (SCr) criteria [AKIN 2015] [Mehta et al. 2007], in patients undergoing CECT with iodixanol vs patients receiving placebo and undergoing nonenhanced computed tomography (NECT) and an additional non* contrast-enhanced ultrasound imaging modality.
Secondary Objectives:

* To demonstrate the safety of i.v. iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in CECT for CKD stage III/IV patients by evaluating the incidence of AKI stage *2, per AKIN SCr criteria [AKIN 2015] [Mehta et al. 2007], in patients undergoing CECT with iodixanol vs patients receiving placebo and undergoing NECT and an additional non*contrast-enhanced ultrasound imaging modality.
* To demonstrate the safety of i.v. iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in CECT for CKD stage III/IV patients by evaluating the incidence of AKI by other definitions (standard definition of contrast induced nephropathy (CIN) [Mehran and Nikolsky 2006], and AKI stages *2 by Waikar criteria [Waikar and Bonventre 2009]) in patients undergoing CECT with iodixanol vs patients receiving placebo and undergoing NECT and an additional non*contrast-enhanced ultrasound imaging modality.
* To demonstrate the safety of i.v. iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in CECT for CKD stage III/IV patients by evaluating mortality and morbidity within 6 months of intervention in patients undergoing CECT with iodixanol vs. patients receiving placebo and undergoing NECT and an additional non*contrast-enhanced ultrasound imaging modality.
* To assess image quality/diagnostic confidence of CECT and NECT plus Ultrasound.
Exploratory Objectives:
* To demonstrate the safety of i.v. iodinated iso-osmolar iodixanol (Visipaque* Injection 320 mgI/mL) usage in CECT for CKD stage III/IV patients by comparing the changes in SCr, cystatin C, neutrophil gelatinase-associated lipocalin (N-GAL), and additional NephroCheck® biomarkers (Tissue inhibitor of metalloproteinases-2 [TIMP-2] and Insulin-Like Growth Factor Binding Protein 7 [IGFBP-7]), if available, relevant to AKI in patients undergoing CECT with iodixanol vs patients receiving placebo and undergoing NECT and an additional non*contrast-enhanced ultrasound imaging modality.
* To determine glomerular filtration rate (GFR) by utilizing an optical renal function monitor (ORFM) in a subset of patients.

Study design

This parallel-group, randomized, placebo-controlled study will examine the incidence and severity of AKI in patients with CKD stage III/IV following an i.v. injection of iso-osmolar iodinated contrast material iodixanol (Visipaque* Injection 320 mgI/mL), as compared with patients who did not receive contrast medium during their scheduled post-EVAR surveillance imaging.
The patients will be randomly assigned in a 1:1 ratio to undergo either CECT or NECT for this routine surveillance CT examination. This randomization of EVAR patients is justified by the clinical equipoise between surveillance protocols that are routinely used in the follow-up of this patient population.

Intervention

Patients randomized to the CECT arm will receive 100 mL iodixanol (Visipaque* Injection 320 mgI/mL) prior to the scheduled CT examination.
Patients randomized to the NECT arm will receive 100 mL saline placebo intravenously prior to a scheduled CT examination and supplemental non-contrast duplex ultrasonography imaging examination. The duplex ultrasound imaging procedure will follow NECT scanning, ideally on the same day as the NECT imaging and within 2 days of performing the NECT.

Study burden and risks

After the EVAR procedure, subjects are required to visit the hospital for regular follow-up scans as part of routine care. For CKD, subjects will need to visit for regular blood tests and other procedures as part of your routine care. The study visits are additional to usual care.

In this trial, Visipaque* will be used in line with approved product information and the risks are also clearly described in the Investigator*s Brochure (IB). Potential risks to patients enrolling into this study are believed to be similar to those described in the IB.

The subjects who participate in this study are patients who would be receiving a CT examination as part of their standard care therefore participation in the study provides similar risks and benefits to participants as those managed according to routine clinical practice.
Participation in this study will not increase lifetime exposure to imaging radiation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

(1) Is *18 years of age at the time that written informed consent is obtained.
(2) Is male or is a nonpregnant, nonlactating female who is either surgically sterile (has a documented bilateral tubal ligation or oophorectomy and/or documented hysterectomy) or is postmenopausal (cessation of menses for more than 1 year). Women of childbearing potential must use adequate contraception* from Screening until 30 days after the Baseline Visit and must have a negative result for a urine human chorionic gonadotropin pregnancy test at the Baseline Visit.
(3) Is an outpatient who has undergone successful EVAR and is scheduled for his/her next post-procedural imaging follow-up examination.
(4) Has previously completed one or more of his or her post-EVAR surveillance imaging examination(s) that provided evidence on stable post-EVAR status.
(5) Has a documented diagnosis of stage III or IV (defined as 30* estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m² and 15 *eGFR <30 mL/min/1.73 m², respectively, according to the Modification of Diet in Renal Disease [MDRD] equation) CKD and stable renal function (last 2 SCr values within ±0.5 mg/dL of each other, with the most recent value within 7 days prior to the scheduled CT examination and the preceding value within 1 to 12 months before that).
(6) Is able to provide written informed consent.
(7) Is able and willing to comply with all study procedures as described in the protocol.
* Adequate contraception is based on those methods identified in the Clinical Trial Facilitation Group document [CTFG Guidance 2014] for clarification of effective contraception. Such methods include: combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal); progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, or implantable); intrauterine device; intrauterine hormone-releasing system; bilateral tubal occlusion; vasectomized partner; sexual abstinence, progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mode of action, male or female condom with or without spermicide cap, diaphragm or sponge with spermicide (refer to protocol Section 8.6).

Exclusion criteria

Patients must be excluded from participating in this study if they meet any of the following criteria
(1) Is pregnant, lactating, is possibly pregnant, or is actively trying to conceive during the study period.
(2) Is a patient for whom an endoleak or other clinically meaningful EVAR-related complication (as
judged by the investigator) has already been discovered.
(3) Is a patient who is undergoing surveillance following a Thoracic Endovascular Repair (TEVAR)
(4) Has a known or suspected history of immediate or delayed hypersensitivity (including but not limited to hives, anaphylactoid or cardiovascular reactions, laryngeal edema, and bronchospasm) to iodine or any iodinated contrast medium.
(5) Is using metformin (e.g., Glucophage®) that cannot be discontinued for the period of 48 hours prior to the Baseline Visit and for at least 48 hours after the imaging procedure (renal function must be evaluated before metformin is resumed).
(6) Has been exposed to any intravascular iodinated contrast medium in the 7 days prior to the Baseline Visit.
(7) Has congestive heart failure (New York Heart Association [NYHA] Class IV) or hepatic failure/liver cirrhosis according to the investigator*s judgement.
(8) Has stage V CKD, defined as eGFR <15 mL/min/1.73 m^2 according to the MDRD equation.
(9) Has a pre-existing requirement for renal dialysis.
(10) Has undergone percutaneous transluminal renal angioplasty (PTRA) within 12 months before the index EVAR procedure or is scheduled to undergo PTRA during the study period.
(11) Has any clinically active, serious, life-threatening disease, medical, or significant psychiatric condition; has a life expectancy of less than 6 months; or is, in the Investigator's opinion, unsuitable for participation in the study for any reason.
(12) Has been enrolled in another clinical study within the 30 days prior to the Screening Visit or is planned to enroll in another clinical study within the duration of this study.
(13) Has been previously enrolled in this study.
(14) Is using i.v. vasopressor or inotropic medications.
(15) Has used nonsteroidal anti-inflammatory drugs (NSAIDs) or any nephrotoxic medication within 48 hours of the Baseline Visit or will do so within 72 hours after the CT procedure (renal function must be evaluated before any nephrotoxic medication is resumed) * with the exception of acetylsalicylic acid (Aspirin) at a dose of *100 mg daily (QD).
(16) Has been hospitalized within 30 days prior to Screening Visit for any reason other than practical purposes for management of tests or diagnostic assessments.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	15
Type:	Anticipated

Ethics review

Approved WMO Date:	08-05-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-10-2018
Application type:	First submission
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	EUCTR2016-001668-13-NL
ClinicalTrials.gov	NCT03119662
CCMO	NL65473.100.18