A Phase 3, Randomized, Double-blind, Placebo Controlled Study to Evaluate the Efficacy and Safety of QPI-1002 for Prevention of Delayed Graft Function in Recipients of a Donation After Brain Death Older Donor Kidney Transplant

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1. To determine the efficacy of QPI-1002 to reduce the incidence and severity of delayed graft function in comparison to placebo in recipients of a donation after brain death (DBD) older donor kidney.2. To assess the safety and tolerability of QPI-...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Renal and urinary tract therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON43248

Source
ToetsingOnline

Brief title
QPI-1002 Phase 3 DGF (ReGIFT)

Condition

- Renal and urinary tract therapeutic procedures

Synonym
"kidney graft dysfunction after kidney transplant" and "kidney not working properly after kidney transplant"

Research involving
Human

Sponsors and support

Primary sponsor: Quark Pharmaceuticals, Inc
Source(s) of monetary or material Support: sponsor;Quark

Intervention

Keyword: Delayed Graft Function, iRNA, Renal Transplant

Outcome measures

Primary outcome

1. The primary endpoint for the study is delayed graft function (DGF) , defined as the as the number of dialysis sessions through Day 30 for subjects who started dialysis beginning in the first 7 days posttransplant.

a. Dialysis sessions will be counted through Day 30 post-transplant, or until a 7 day dialysis free period occurs, whichever occurs first. Individual hemo- or peritoneal dialysis sessions will be counted individually. Subjects who receive continuous peritoneal filtration will count as 3 sessions/week. Continuous hemofiltration will also be counted as 3 sessions/week.

b. A subject who does not have DGF (i.e., dialysis in the first 7 days post-transplant) will be classified as having 0 dialysis sessions.

c. Subjects who drop out on or before Day 7, regardless of the reason for dropout (e.g., experience primary non-function (PNF), graft loss, death or lost-to-follow up), will be considered to have failed the primary endpoint and will be assigned the maximum number of dialysis sessions from the day of dropout. Dialysis session is defined in the protocol. The maximum number of dialysis sessions will be the observed number of dialysis sessions (to the

point of drop out or loss) plus 3 dialysis sessions per week from that point to Day 30. This reflects the typical practice of administration of 3 dialysis sessions per week inclusive of the actual number of dialysis sessions observed. PNF is defined for efficacy analysis as continuous requirement for dialysis starting in the first 7 days after transplant and lasting for at least 60 days post-transplant.

Secondary outcome

Key Secondary Endpoints:

1. The proportion of subjects requiring dialysis for any reason in the first 7 days post-transplant.[2]

2. The proportion of subjects with a fall in serum creatinine of * 10% on three consecutive days in the first 7 days post-transplant.[3]

Other Secondary Endpoints:

1. The proportion of subjects with DGF defined as the need for acute dialysis within the first 7 days posttransplant, excluding the following:

a. Dialysis performed during the first 24 hours for the treatment of hyperkalemia or hypervolemia

b. Dialysis performed during the first 7 days post-transplant for one or more of the following reasons:

1) Obstructive uropathy (determined radiologically)

2) Fulminant recurrence of primary disease (underlying etiology of ESRD), including focal segmental glomerulosclerosis

3) Biopsy confirmed thrombotic microangiopathy (Thrombotic Thrombocytopenic

Purpura or Hemolytic*Uremic Syndrome)

4) Hyperacute rejection or other antibody-mediated acute rejection

5) Technical vascular complications involving the allograft: renal arterial and/or venous thrombosis due to vascular injury or technical surgical complications.

2. The proportion of patients requiring any dialysis in the first 30 days.

3. Time to first dialysis.

4. Duration of DGF in those subjects with DGF.

5. The proportion of subjects with a serum creatinine > 3 mg/dL but who have not required dialysis by Day 5 post-transplant (traditional definition of slow graft function).

6. Creatinine reduction ratio on Study Day 2 (SCRR2)[4] compared to Study Day 1 for those subjects without DGF.

7. Change from baseline in serum creatinine and eGFR (as determined from the (a) 4-variable MDRD equation[5] and (b) Cockcroft-Gault equation[6] after adjustment per 1.73 m2 body surface) at Days 1, 2, 3, 4, 5, 7, 14, 30, 60, 90 and 180.

8. Rate of change in renal function (slope) in serum creatinine and eGFR (as determined from the (a) 4-variable MDRD equation and (b) Cockcroft-Gault equation after adjustment per 1.73 m2 body surface) at Days 1, 2, 3, 4, 7, 14, 30, 60, 90 and 180.

9. Mean serum creatinine and mean eGFR (as determined from the (a) 4-variable MDRD equation and (b) Cockcroft-Gault equation after adjustment per 1.73 m2 body surface at Day 1, 2, 3, 4, 7, 14, 60, 90 and 180.

10. Proportion of patients with eGFR * 60 mL/min/1.73 m2 (as determined from the (a) 4-variable MDRD equation and (b) Cockcroft-Gault equation after adjustment per 1.73 m2 body surface) at Day 90 and Day 180 (6 months).

11. Total urine output (volume) during the initial 24 hours and Day 3 post-transplant.

12. Length of transplant hospitalization (days).

13. Number of hospital readmissions and total number of hospital days through Day 90 and Day 180.

14. Kidney Disease Quality of Life * Short Form (KDQOL-SF*).

Study description

Background summary

See protocol p23 - 36

1.1 Drug Product and Proposed Indication
QPI-1002 is a nuclease-resistant, synthetic double-stranded RNA oligonucleotide designed to temporarily inhibit the expression of the pro-apoptotic gene, p53, via activation of the RNA interference (RNAi) pathway. QPI-1002 has been evaluated in a large Phase1/2 study:
Controlled, Randomized Prospective, Double-Blind, Multicenter Phase1/2, Dose-Escalation Study of the Safety, PK, and Clinical Activity of I5NP for Prophylaxis of Delayed Graft Function in Patients Undergoing Decreased Donor Kidney Transplantation (QRK006).
QPI-1002 is being developed for reduction in the incidence and severity of delayed graft function (DGF) in patients receiving renal transplants.

1.2 Nonclinical Studies
QPI-1002 is rapidly cleared from the plasma and accumulates to appreciable levels only in the kidney. Following IV administration of QPI-1002, the majority of the drug is cleared rapidly from the plasma by kidney filtration and a small proportion is reabsorbed by the proximal tubules, with the rest being excreted in the urine. Two-photon microscopy studies indicate that QPI-1002 uptake by the kidney occurs mostly through re-absorption of QPI-1002 from the glomerular filtrate. The results of the nonclinical toxicology program

indicated that there are no significant issues that would preclude evaluation of IV administration of QPI-1002 in humans. The nonclinical studies are described in the Investigator*s Brochure.

1.3 Background of Disease:
Role of p53 and Donor Age The etiology of DGF appears to be primarily related to ischemia-reperfusion (IR) injury.
Renal tubular epithelial cell dysfunction and apoptotic cell death are the hallmarks of this process.[8] The expression of p53 is upregulated within 24 hours of injury in the rat IR model of acute kidney injury.[9] Activation of the pro-apoptotic p53 protein was found to be a reliable marker for cellular damage in human renal biopsies.[10] Increased p53 protein was also identified in *zero hour* human kidney biopsies from deceased donors whose recipients had DGF post-transplant.
No significant increase of p53 in living donors or deceased donor transplant recipients without DGF was found.[11]
Following ischemic injury, proximal tubular cells (PTC) die in a p53-dependent manner[12] or enter a p53-dependent G2 type of cell cycle arrest, do not proliferate effectively, and begin secreting pro-fibrotic factors. This favors fibroblast proliferation and fibrosis rather than regenerative type of wound healing.[13] These early pro-fibrotic events following acute renal injury appear to contribute to late outcomes such as chronic allograft nephropathy, as demonstrated in animal models and human histological studies.[13-15] The rationale for temporary therapeutic inhibition of p53 activity for amelioration of DGF following kidney transplantation is thus two-fold. First, by blocking p53-dependent apoptosis, it may afford
PTC the opportunity to repair their cellular damage and avoid massive cell death in response to the injury, thus preserving the organ integrity and functionality.[16] Secondly, blocking p53-dependent prolonged G2 arrest may favor regenerative rather than fibrotic type of renal wound healing. In accordance with this concept, preclinical renal transplant models with an analogue of QPI-1002 have demonstrated efficacy in reducing injury.[17] In kidney transplant patients, the rationale for the temporary inhibition of p53 expression by QPI-1002 is that it affords kidney cells time to repair cellular damage and therefore avoid induction of apoptosis. Cells that are too damaged, or that have accumulated deleterious mutations, are later eradicated when the effects of QPI-1002 have subsided and p53 expression levels return to normal.[18] In rat kidneys, p53 expression levels returned to normal between 2-3 days after intravenous administration of a rat analogue of QPI-1002.
Another clinically relevant attribute observed in the preclinical studies was that treatment with siRNA targeting p53 could be administered up to 4 hours after the ischemic reperfusion injury.
Recent preclinical data also indicate that p53 activation in ischemia-reperfusion injury is greater in older kidneys[19,20] (Figure 1-1). Thus, treatment of recipients of older kidneys with a p53 inhibitor is expected to yield a greater beneficial effect than in recipients of younger donor organs. Donor organ age has a direct impact on outcomes in renal transplantation. Due

to the growing disparity between the numbers of candidates awaiting transplantation and available donor organs, the use of kidneys from older donors, such as extended criteria donors (ECD) have been used.[21] Patients who receive ECD kidneys exhibit higher rates of DGF, experience longer lengths of stay during the transplant hospitalization, and are also readmitted more frequently thereafter than those receiving grafts from standard criteria donors (SCDs).[22] In a recent review of the United Network of Organ Sharing (UNOS) database, the incidence of DGF in ECD kidneys was 36% compared to 24% for non-ECD kidneys.[23] Concerns over risk of DGF development in older kidney grafts affects medical decision-making and contributes to higher organ discard rates. Donor age has been suggested to be the most potent donor risk factor and a surrogate measure of kidney quality for physiologic reasons, including increased comorbidities and greater vulnerability to ischemic injury.[24] Published data show a direct correlation between increasing kidney donor age and organ discard rates.[25]

1.4 Background of Disease: DGF Severity
In a recent review, eighteen different clinical definitions of DGF were identified in literature published since 2000, reflective of a lack of consensus within the transplant community regarding this condition.[2] Ten different methods to diagnose or identify DGF were also noted, including several different approaches to the assessment of the rate of recovery of renal function following reperfusion of the allograft.[24,26] Efforts to assess acute kidney injury and function are confounded by a number of clinical variables, including the timing of pre-transplant dialysis in relation to transplant surgery, and intra- and post-operative management of the patient. The endpoints used in DGF studies can be grouped into two categories: those based upon the need for dialysis and those based upon the rate of recovery of renal function following transplantation. Non-dialysis definitions of DGF that have been proposed include:
1) DGF defined as present if serum creatinine levels increased, remained unchanged, or decreased less than 10% per day for three consecutive days in the first week after transplantation[3]; 2) a 24 hr urinary creatinine excretion < 1000 mg during the first postoperative day[4]; 3) a length of time of > 6 days needed to achieve a level of renal function corresponding to a creatinine clearance > 10 mL/min[27]; and 4) in patients not receiving dialysis, a serum creatinine reduction ratio on Day 2 versus Day 1 (SCRR2) < 30% (nondialysis DGF, nd-DGF).[28] DGF is most commonly defined as the need for dialysis within the first seven days after transplantation, as used by the UNOS, which has been shown to be associated with poorer graft function and survival.[2]
While the simple dichotomy of an incidence of dialysis-based endpoints such as the UNOS endpoint has had predominant use in clinical trials, it is unable to discriminate between clinically important aspects of DGF, such as the difference between a short course of dialysis to support a patient during DGF versus a long course. Recently, data have been presented that support a more discriminating functional endpoint that is less subjective and less variable than the decision to dialyze a patient in the first week post-transplant,

allowing prediction of outcomes based on the amount of post-transplant dialysis. This endpoint, known as DGF severity, is defined as the number of dialysis sessions required immediately posttransplant.[29-32] Schnuelle et al., evaluated 300 consecutive DBD transplants performed at a single center in Germany from 1998 to 2005.[32] It was observed that there was a significant relationship between both duration of dialysis in days and duration measured as dialysis session counts and graft survival.

Marek et al., evaluated outcomes of three groups based on need for dialysis: 1) less than 7 days (n = 52); 2) 7-14 days (n = 13; and 3) > 14 days (n = 18). Creatinine clearance was significantly different among the three groups at 30 days (42.5, 33.8, and 20 mL/min, respectively, $p < 0.001$) and at 1 year (56.7, 49.2, and 37.3 mL/min, respectively, $p = 0.031$). A multivariate regression analysis identified time needed on dialysis as a significant predictors of creatinine clearance at 1 year.[31] Buchanan et al., analyzed data from the U.S. Renal Data System (USRDS).[30] Graft survival rates varied significantly based on post-transplant dialysis utilization with the worst outcomes occurring in those with DGF and requiring dialysis beyond the first week posttransplant. Akkina et al., analyzed the incidence and clinical correlates of DGF (defined as need for dialysis in the first week after transplant) and long-term outcomes from 5072 adult kidney only transplants performed at 2 centers from 1984-2006.[29] The severity of DGF, as defined by the number of dialysis treatments, was associated with graft failure. Short DGF (1*2 dialysis treatments) was associated with a 27% higher risk of graft failure. Prolonged DGF (* 3 dialysis treatments) was associated with an increased risk of graft failure (51%). Schneulle et al., also showed that DGF requiring > 2 dialysis treatments (N = 78) was associated with worsened graft survival compared to both immediate function (N = 189) and DGF requiring only 1*2 dialysis treatments (N = 43). These studies indicate that small increments in post-transplant dialysis are associated with worsening clinical outcomes.[32]

The relationship between DGF risk score and severity of DGF was evaluated based on data from the QRK006 Phase 2 study (placebo group) (Squiers et al., AJT 2015).[33] This relationship was quantified using the negative binomial model. Using the DGF risk prediction model[34] based on the UNOS registry, association of DGF risk and long-term graft failure, the relative impact of the severity of DGF on long-term graft failure can be inferred. A change in dialysis sessions per subject from 0.5 to 1.5 (range: 0.9 to 2.8), increased the risk of graft failure and reduced 3 year graft survival by 9%. With a further increase in the number of dialysis sessions to 6.6 sessions per subject (range: 3.5 to > 10 per subject) a 16% decrease in graft survival at 3 years post-transplant was observed compared with 0.5 dialysis sessions per subject.

This analysis, along with the other published studies[29-32] supports that not just having DGF, but each additional dialysis session during early post-transplant period, is clinically meaningful and is associated with poorer outcomes following transplantation. The impact of each individual dialysis is not unexpected as each dialysis carries a risk of transient ischemia, inducing further damage to the kidneys, which have a variable degree of existing damage and is also reflective of the degree of injury of the deceased donor organ.

Such analyses indicate that each additional dialysis session increases disease burden, leading to poor graft survival, a clinically meaningful outcome for the transplant patient and health care providers.
The mean number of dialysis sessions for patients treated with placebo in the QRK006 Part B study was 2.3 sessions when including all patients (assigning a value of 0 to patients who did not develop DGF) and 4.6 when only including patients who experienced DGF. Reducing these values by 40% (the percent decrease used to power the study) would reduce the number of dialysis sessions by approximately 0.92 when including all patients by 1.84 dialysis sessions when only including patients who experienced DGF. Both of these reductions are well within the range predicted by the literature and by the DGF risk prediction model to be important in predicting long-term outcome. Even lesser reductions in the range of 30% would be expected to yield clinically significant improvements on long-term outcome.

Study objective

1. To determine the efficacy of QPI-1002 to reduce the incidence and severity of delayed graft function in comparison to placebo in recipients of a donation after brain death (DBD) older donor kidney.
2. To assess the safety and tolerability of QPI-1002 in comparison to placebo when administered to recipients of a DBD donor kidney.

Study design

This is a Phase 3 randomized, placebo-controlled, double-blind, multi-center trial stratified by donor age (45-59 years vs * 60 years) and by region to evaluate the reduction in incidence and severity of delayed graft function with kidney allografts from DBD donors who were at least 45 years of age.

Intervention

This is a single dose treatment protocol. Subjects who meet all eligibility criteria will be randomized 1:1 within 48 hours prior to transplant surgery to receive a blinded single infusion of either QPI-1002 (10mg/kg) or placebo.

Study burden and risks

See IB - 5.5 Evaluation of the Benefit-Risk Ratio
Unblinded review by the Sponsor and DSMB of the Phase 1 safety data for QPI-1002 (AEs, ECGs, laboratory data) did not indicate the presence of any dose related toxicity. From the Phase 2 study in DGF (N = 332), based on the evaluation of safety in the QPI-1002 and Placebo treatment groups, the cumulative frequencies and types of adverse events reported were those expected among patients with ESRD undergoing deceased donor renal transplantation. Events such as anemia, complications of kidney transplant and hyperkalemia are

expected during the perioperative period, in particular, with transplantation of ECD kidneys and those SCD kidneys with prolonged cold ischemia times, where DGF or slower recovery of graft function is more common.
The overall frequency and severity distribution of AEs was similar in both treatment arms, and nearly all events (99.6%) were assessed by investigators as not related, or unlikely to be related, to study drug.
As was observed for adverse events, the observed patterns of abnormal safety laboratory results was typical of an adult ESRD population. This was seen in terms of the generally moderate degree of reduction in blood hemoglobin levels, the transient increase in WBC count as an acute phase reactant during the early postoperative period, and the observed electrolyte and metabolic disturbances and pre-transplant elevations in serum amylase and/or lipase. Variable, mild to moderate, but transient elevations in hepatic transaminase levels were observed in both treatment groups and did not differ significantly between them. None of these elevations were associated with de novo elevations in serum total bilirubin, and there were no cases identified, by individual investigators or by the Sponsor, that met the Hy*s Law Criteria for potential drug-associated hepatotoxicity. Indices of pancreatic function, notably serum amylase and lipase levels, tended, in some cases, to increase perioperatively for reasons that remain unclear. However, the elevations were always transient and the magnitude, as reflected by changes in mean and median blood levels, was similar in the QPI-1002- and Placebo treatment groups.
In both treatment arms, the cumulative rates of acute rejection at 6 months post-transplant* 15.6% and 15.9% in the QPI-1002 and Placebo groups, respectively, were consistent with published rates of rejection of high risk kidney transplants.[72]
On the basis of the single SAE reported as related (Myocardial Infarction) in QRK006 Part B, the Sponsor examined the events reported in the cardiac SOC for evaluation of potential signals, as well as the Embolic and Thrombotic event SMQ. Both serious and non-serious events at the SOC and SMQ level and PT levels included in the SOC and SMQ were similar between treatment groups and no safety signal was identified. Additional review of events corresponding to nonclinical toxicology findings was performed post hoc.
An equal number (n = 89) of patients in each treatment group reported events corresponding to the gastrointestinal SOC, with no events of gastric ulceration reported so there was no clinical events, and no suggestion of a safety signal, corresponding to the non-clinical reports of erosion/ulcers of the stomach following QPI-1002 treatment. No adverse events that would correspond to thymic hemorrhage or lymphoid hyperplasia as seen in the nonclinical toxicology were reported, and no PTLD was reported in the study.
The overall frequency and type of AEs of special interest including rejection, serious infections such as those associated with CMV, and BK virus, and malignancies reported were typical for the population of ESRD patients under study and did not differ between treatment groups. Over the time period of the study for which data is available (2008-20012), graft loss or death was reported in 4.8-6.3% of deceased donor kidneys overall (2012 SRTR) and the 6-month allograft and patient survival rates were similar to those in the

published literature[72] and did not differ between the treatment groups.
In summary, when administered to ESRD patients undergoing transplantation of expanded criteria donor kidneys, the single-dose, IV bolus administration of QPI-1002 demonstrated a safety profile comparable to that of isotonic saline placebo. There have been no identified or validated safety signals from the administration of QPI-1002 and thus no defined risks associated with QPI-1002 compared to placebo control in the populations evaluated to date. The benefit * risk of QPI-1002 is acceptable for further investigation in the reduction in the incidence and severity of delayed graft function (DGF) among recipients of kidney transplant from deceased donors, and for the prevention of acute kidney injury (AKI) in patients undergoing cardiovascular surgery.

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. Has the ability to understand the requirements of the study, is able to provide written informed consent (including consent for the use and disclosure of research related health information) and is willing and able to comply with the requirements of the study protocol (including required study visits).
2. Male or female at least 18 years of age.
3. Has dialysis dependent renal failure initiated at least 2 months prior to transplantation.
4. Is to be a recipient of a transplant from a deceased donor (brain death criteria) * 45 years of age.
5. Based on donor age, the following requirements for the risk of DGF (determined using the Irish DGF risk assessment nomogram) and cold ischemia time (CIT) must be met:
a. Donor age 45 * 59 years: estimated DGF risk * 20% and estimated CIT *10 hour
b. Donor age * 60 years: no minimum estimated DGF risk or minimum estimated CIT
6. Is able to comply with the requirement of antibody induction therapy with rabbit polyclonal anti-thymocyte globulin or anti-CD25 (anti-IL2R) monoclonal antibodies per center standard of care.
7. A female subject is eligible to enter the study if she is:
a. Not pregnant or nursing
b. Of non-childbearing potential (i.e., post-menopausal defined as having been amenorrheic for at least 1 year prior to screening, or has had a bilateral tubal ligation at least 6 months prior to administration of study drug or bilateral oophorectomy or complete hysterectomy).
c. If of childbearing potential, must have a negative serum or urine pregnancy test within 48 hours prior to transplant surgery and be using an effective means of contraception (per the site-specific guidelines or using 2 methods of birth control concurrently, whichever is more stringent) which will be continued until the Day 180 visit.
8. Male subjects with female partners of childbearing potential must agree to use an effective means of contraception (per the site-specific guidelines or use 2 methods of birth control concurrently, whichever is more stringent), which will be continued until the Day 180 visit.
9. Must be up-to-date on cancer screening according to site-specific guidelines and past medical history must be negative for biopsy-confirmed malignancy within 5 years of randomization, with the exception of adequately treated basal cell or squamous cell carcinoma in situ or carcinoma of the cervix in situ.

Exclusion criteria

1. Recipient of a live donor kidney or a kidney from a donation after cardiac death (DCD) donor.
2. Recipient of donor kidney preserved with normothermic machine perfusion.
3. Scheduled to undergo multiorgan transplantation.
4. Has a planned transplant of kidneys that are implanted en bloc (dual kidney transplant).
5. Has planned transplant of dual kidneys (from the same donor) transplanted not en bloc.
6. Has lost first kidney transplant due to graft thrombosis.
7. Is scheduled for transplantation of a kidney from a donor who is known to have received an

investigational therapy under another IND/CTA for ischemic/ reperfusion injury immediately prior to organ recovery.
8. Is scheduled to receive an ABO-incompatible donor kidney.
9. Has a positive T- or B-cell cross-match by NIH anti-globulin lymphocytotoxicity method or CDC cross-match method, if performed.
10. Has a positive T- or B-cell flow cross-match AND donor specific anti-HLA antibody (DSA) detected by flow cytometry, Luminex® based antigen-specific anti-HLA antibody testing, or by similar methodology, if performed.
11. Has undergone desensitization to remove donor specific anti-HLA antibodies prior to transplantation.
12. Has participated in an investigational study within the last 30 days or received an investigational product within 5 half-lives of the study drug administration, whichever is longest.
13. Has known allergy to or has participated in a prior study with siRNA.
14. Has a history of HBV (Note: subjects with a serological profile suggestive of clearance, or prior antiviral treatment of a prior HBV infection, may be enrolled with the approval of the Medical Monitor).
15. Has a history of HIV.
16. Recipient of a known HIV positive donor kidney.
17. Is HCV-positive (detectable HCV RNA) (Note: Subjects at least 24 weeks from completion of treatment with an approved antiviral regimen and who remain free of HCV as determined by HCV RNA testing may be enrolled. Subjects who have been cleared of HCV virus after treatment with an unapproved regimen should be approved by the Medical Monitor).
18. Has history or presence of a medical condition or disease or psychiatric condition that in the investigator's assessment would place the patient at an unacceptable risk for study participation.

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:	Prevention

Recruitment

NL

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

Ethics review

Approved WMO Date:	16-09-2016
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-02-2017
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2015-003078-33-NL
ClinicalTrials.gov	NCT02610296
CCMO	NL57884.000.16