Silencing inflammatory activity by injecting Nanocort in patients at risk for atherosclerotic disease.

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Nanocort reduces vascular inflammation in patients at risk for atherosclerotic events.

Ethische beoordeling	Niet van toepassing
Status	Werving gestopt
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON25109

Bron
NTR

Verkorte titel
SILENCE

Aandoening

Atherosclerosis
vaatverkalking

Ondersteuning

Primaire sponsor: Dept of vascular medicine, Academic Medical Center
Overige ondersteuning: fund = initiator = sponser

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To evaluate the effects of short-term liposomal glucocorticoid (Nanocort) infusion on

atherosclerotic plaque inflammation in humans measured by 18FDG PET/CT.

Toelichting onderzoek

Achtergrond van het onderzoek

Cardiovascular disease(CVD) is the leading cause of morbidity and mortality in developed nations. CVD is primarily caused by atherosclerosis, a systemic disease characterized by lipid deposition in the subendothelial space with a concomitant, low-grade inflammatory reaction.(Fuster, Moreno et al. 2005) To date, most therapeutic interventions aimed at lowering CVD have thus far focused on modulating lipid levels, either lowering LDLc or increasing HDLc levels. Yet, since the introduction of statins 20 years ago, there have been few breakthroughs in the treatment of this disease. A promising strategy to reduce CVD is to directly target inflammation at the level of the vessel wall.(van Leuven, van Wijk et al.; Libby 2002) A potential drawback of anti-inflammatory strategies pertains to the thin line between inhibiting ‘inappropriate’ inflammation versus inducing immuno-suppression. Therfore, continous low dosed anti-inflammatory drugs have great potential as novel treatment trategies. In the present project, we propose to inject liposomal glucocorticoids intravenously in patients with an risk of atherosclerotic disease aiming to reduce vessel wall inflammation as measured with FDG-PET.

Doel van het onderzoek

Nanocort reduces vascular inflammation in patients at risk for atherosclerotic events.

Onderzoeksopzet

The study will consist of:

1. A pre-randomization 18FDG PET/CT and a baseline MRI. (from Day -14 to Day 1);

2. Day 1 IV infusion with Nanocort or placebo control (Saline);

3. Day 8 IV infusion with Nanocort or placebo control;

4. Day 12 (± 3 days) 18FDG PET/CT with a subsequent close-out visit.

Total study time will be maximally 29 days, including the screening visit.

Onderzoeksproduct en/of interventie

Two weekly IV infusions of 150 mg Nanocort (PEG-liposomal prednisolone sodium phosphate).

or a placebo (Saline solution; same solution brand as used to dilute/prepare Nanocort injection).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Patients must meet the following criteria for study entry:

1. Male patients aged equal to or greater than (≥) 60 years;

2. Evidence of qualifying vessel (carotid or aortic) plaque inflammation defined as Target (Plaque) to Background (Blood) ratio (TBR) > 2.2, (calculated using the mean of the maximum SUV) as measured by 18FDG PET/CT;

3. Known with an elevated risk factor for cardiovascular disease for example, but not limited to:

A. Body Mass Index > 26;

B. Elevated blood pressure (> 135/85);

C. Central obesity (according to “New International Diabetes Federation definition”);

D. Reduced High density lipoprotein (HDL<1.03 mmol/L).

4. If using a statin, on stable therapy for at least 6 weeks prior to screening with no evidence of statin intolerance;

5. For patients taking angiotensin-converting enzyme (ACE) inhibitors (ACE-I) or angiotensin-receptor blockers (ARBs), non-statin lipid-modifying therapy, thiazolidinediones, inhaled steroids, or leukotriene modifying agents, use of a stable dose for at least 6 weeks prior to baseline measurement;

6. Stable Nonsteroidal anti-inflammatory drugs (NSAIDS), Cyclo-oxygenase-2 inhibitors (COXIBs) for at least 6 weeks prior to baseline measurement;

7. Subject agrees to the restrictions as described in paragraph 4.6. In brief: Subjects are not permitted any alcohol or caffeine-containing food or drinks from 12 hrs prior to study visits until discharge. In addition, no strenuous exercise is permitted for 24 hrs before the study visits.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

Subjects may not enter this study if they meet the following criteria:

1. Current medical history of Auto-immune disease/vasculitis, active inflammatory diseases, proven or suspected bacterial infections. Recent (<1 month prior to screening) or ongoing serious infection requiring IV antibiotic therapy;

2. Recent or current treatment with medications that may have a significant effect on plaque inflammation as measured by plaque TBR, including but not limited to:

A. Steroids for at least 6 weeks prior to baseline measurement and during study (with the exception of inhaled steroids);

B. Biological based medicines (anti-TNF (ex. Infliximab), anti-IL-6 therapy (ex. Tocilizumab) or anti-IL-1 (ex. anakinra)) within 8 weeks before the baseline visit and during the study;

C. No other Disease modifying antirheumatic drugs (DMRADS) within 6 weeks of baseline and during study (such as cyclosporine, azatioprine, etc.).

3. Known systemic disorders such as hepatic, renal, hematologic, and malignant diseases or any clinically significant medical condition that could interfere with the conduct of the study;

4. Standard contra-indications to MRI, 18FDG PET, and CT;

5. Current medical history of poorly controlled diabetes defined as hemoglobin A1c (HbA1c) >7.5%;

6. History of anaphylaxis, anaphylactoid (resembling anaphylaxis) reactions, or severe allergic responses;

7. Inability or unwillingness to comply with the protocol requirements, or deemed by investigator to be unfit for the study;

8. Subject has planned cardiac surgery, PCI or carotid stenting, or major non-cardiac surgery during the course of the study period or for 14 days after the last treatment;

9. Current medical history of drug or alcohol abuse within 12 months prior to screening;

10. Subjects are not permitted to enter the study if they have taken any investigational drug in the 3 months prior to study drug administration;

11. Subjects are not permitted to enter the study if they have taken insulin or any oral anti-diabetic (except metformin) in the last 30 days. Those subjects who are taking metformin may be included in the study if they are on a stable dose for at least 4 weeks and have a HbA1c <7.5%.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Dubbelblind
Controle:	Placebo

Deelname

Nederland

Status:	Werving gestopt
(Verwachte) startdatum:	01-09-2011
Aantal proefpersonen:	90
Type:	Werkelijke startdatum

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2796
NTR-old	NTR2936
Ander register	AMC : 2011-002686-37
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Resultaten

Samenvatting resultaten
N/A