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

No registrations found.

| | |
|---|---|
| **Ethical review** | Not applicable |
| **Status** | Recruitment stopped |
| **Health condition type** | - |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON25109

**Source**
NTR

**Brief title**
SILENCE

**Health condition**

Atherosclerosis
vaatverkalking

### Sponsors and support

**Primary sponsor:** Dept of vascular medicine, Academic Medical Center
**Source(s) of monetary or material Support:** fund = initiator = sponser

### Intervention

### Outcome measures

**Primary outcome**

To evaluate the effects of short-term liposomal glucocorticoid (Nanocort) infusion on atherosclerotic plaque inflammation in humans measured by 18FDG PET/CT.

### Secondary outcome

1. To study the effect of Nanocort infusion on plaque neovascularisation and endothelial permeability (DCE-MRI) of the carotid arteries and/or aorta;

2. To evaluate the effect of Nanocort infusion on inflammatory markers.

## Study description

### Background summary

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.

### Study objective

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

### Study design

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.

**Intervention**

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).

# Contacts

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# Eligibility criteria

## Inclusion criteria

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.

## Exclusion criteria

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%.

# Study design

## Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-09-2011 |
| Enrollment: | 90 |
| Type: | Actual |

# Ethics review

Not applicable
Application type: Not applicable

# 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 |
|---|---|
| NTR-new | NL2796 |
| NTR-old | NTR2936 |
| Other | AMC : 2011-002686-37 |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Study results

**Summary results**
N/A