Specifying the anti-inflammatory effects of ziltivekimab with diverse imaging modalities and in-depth cellular phenotyping

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This study has been transitioned to CTIS with ID 2024-515893-29-01 check the CTIS register for the current data. To study whether ziltivekimab therapy reduces arterial wall inflammation as assessed by imaging, and reduces the systemic inflammatory…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON53495

Source
ToetsingOnline

Brief title
SPIDER

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Atherosclerosis, low-grade inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Vasculaire Geneeskunde
Source(s) of monetary or material Support: Novo Nordisk A/S

Intervention

Keyword: Atherosclerosis, cardiovascular disease, imaging, inflammation

Outcome measures

Primary outcome

The main outcome is the mean percentage change in coronary arteries target to background ratio (TBRmax) and monocyte activation marker protein expression between the treatment and placebo group, at the primary analysis time point of 20 weeks, compared to baseline.

Secondary outcome

Imaging:

• Difference in PCAT (CCTA derived) after ziltivekimab treatment.

• Correlation between changes in coronary 68Ga-DOTATATE uptake and anatomical plaque changes on CCTA.

• Difference in 68Ga-DOTATATE SUVmax of bone marrow and spleen after treatment.

• Difference in 68Ga-DOTATATE TBRmax of ascending aorta after treatment.

Inflammation and proteomics:

• The impact of ziltivekimab on monocyte phenotype in transendothelial migration (TEM) capacity and transcriptome profile.

• The mean percentage change in plasmatic proteins before and after ziltivekimab treatment.

• The impact of ziltivekimab on inflammation in plasma cytokine and chemokine

levels.

Study description

Background summary

Inflammation is an important component in atherogenesis. The pro-inflammatory cytokine interleukin-6 (IL-6) is a pivotal factor in plaque development and rupture. Elevated IL-6 levels lead to more arterial wall inflammation and an increased atherosclerotic cardiovascular disease (ASCVD) risk.
Ziltivekimab is a novel human monoclonal antibody targeting the IL-6 ligand and is in development for ASCVD risk attenuation. Although the safety and efficacy of ziltivekimab has been studied, the mechanistic effects on atherosclerotic plaques and inflammatory pathways have not been investigated in humans to date.
In this study, we aim to unravel the effect of ziltivekimab on arterial wall inflammation and systemic inflammatory tone. The insights will be vital for the future selection of patients that will benefit from ziltivekimab and for the further development of anti-inflammatory therapies for ASCVD.

Study objective

This study has been transitioned to CTIS with ID 2024-515893-29-01 check the CTIS register for the current data.

To study whether ziltivekimab therapy reduces arterial wall inflammation as assessed by imaging, and reduces the systemic inflammatory tone as assessed by circulating monocytes, inflammatory biomarkers and proteomics.

Study design

This study is designed as a randomized, double blind, placebo-controlled trial.

Intervention

Ziltivekimab 15 mg or placebo, subcutaneously delivered using a manual syringe, once per every four weeks, for a total of 20 weeks (6 administrations).

Study burden and risks

Participants will be randomized to either ziltivekimab or placebo and will be subjected to imaging scans and blood withdrawals. To date, ziltivekimab

administration has proven safe and well-tolerated. In theory, a modest increase in infectious disease susceptibility may occur. The study will require a maximum of eight study visits. The blood withdrawal will total 233 ml. The radiation exposure from two 68Ga-DOTATATE PET/CT and two coronary CT angiography (CCTA) scans is maximally estimated at 9.5 mSv. Awaiting the ongoing cardiovascular outcome trial with ziltivekimab in secondary prevention patients, the participating patients will likely not experience direct clinical benefit by anti-inflammatory therapy, but they will contribute to the current knowledge of a potential effective treatment option.

Contacts

Public
Selecteer

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Selecteer

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Aged 50 years and older.

- Multi-vessel coronary artery disease (defined as CAD-RADS >=2 and/or PAV/NCPV stage >=2).
- Serum hsCRP level >=2 mg/L.

Exclusion criteria

- Coronary stents in situ.
- Chronic or recent (<1 month) (serious) infections and/or clinical signs of acute (serious) infection.
- History of severe auto-immune diseases, or other (severe) (recurrent or chronic) inflammatory disorders.
- Untreated latent tuberculosis, active hepatitis B (positive HBsAg and/or positive anti-HBc with detectable HBV DNA) or C, human immunodeficiency virus (HIV) not on stable antiretroviral regimen

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-11-2023
Enrollment:	40
Type:	Actual

Medical products/devices used

Registration:	No

Product type:	Medicine
Brand name:	68Ga-DOTATATE
Generic name:	68Ga-DOTATATE
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Ziltivekimab
Generic name:	Ziltivekimab

Ethics review

Approved WMO Date:	27-07-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-04-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-515893-29-01
EudraCT	EUCTR2022-004078-53-NL
CCMO	NL83403.018.22