CD8 T cell imaging by positron emission tomography with 89Zr-Df-IAB22M2C in giant cell arteritis and rheumatoid arthritis: a pilot study

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Primary Objective: to evaluate arterial or synovial 89Zr-Df-crefmirlimab uptake on PET/CT in patients with GCA or RASecondary objectives are:1. Assessment of the relationship between 89Zr-Df-crefmirlimab uptake and the presence of CD8 T cells in...

Ethical review	Approved WMO
Status	Pending
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON53860

Source
ToetsingOnline

Brief title
CD8 T cell PET in GCA and RA

Condition

- Autoimmune disorders
- Synovial and bursal disorders
- Vascular disorders NEC

Synonym
giant cell arteritis (vasculitis), rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Europese Unie

Intervention

Keyword: CD8 T cell, giant cell arteritis (GCA), PETCT, rheumatoid arthritis (RA)

Outcome measures

Primary outcome

Main study endpoints: The main endpoints are arterial 89Zr-Df-crefmirlimab uptake in patients with newly-diagnosed GCA, and synovial 89Zr-Df-crefmirlimab uptake in patients with active RA.

Secondary outcome

Secondary endpoints include:

1) the relationship between 89Zr-Df-crefmirlimab uptake in temporal arteries and the presence of CD8 T cells in histological analysis of temporal artery biopsy in patients with newly-diagnosed, cranial GCA

2) the relationship between 89Zr-Df-crefmirlimab uptake and clinical joint assessment and histological analysis of synovial tissue in patients with RA.

Study description

Background summary

Giant cell arteritis (GCA) and rheumatoid arthritis (RA) are both auto-immune diseases that are characterized by chronic inflammation of large/medium-sized arteries and joints, respectively. The inflammation in GCA and RA is usually chronic, and may cause progressive damage of the affected tissues if left untreated. However, inappropriate treatment may also pose unnecessary risks for patients due to toxicity of the immunosuppressive treatment. The improvement of early diagnostics and therapy monitoring remains challenging for both diseases.

A new and reliable tool for diagnostics and therapy monitoring of GCA and RA could greatly reduce permanent physical damage due to inflammation, as well as inappropriate use of immunosuppressive treatments.

A new and promising approach to visualize arterial and synovial inflammation might be to combine positron emission tomography (PET) with novel tracers that target specific immune cells in affected tissues. CD8 T cells could be an important target for this novel imaging approach, since these cells are abundantly present in the inflamed arterial wall and synovial tissue of patients with GCA and RA, respectively. Currently, tools are becoming available from oncology studies to visualize CD8 T cells. ImaginAb has developed 89Zr-Df-IAB22M2C, an 80 kDa minibody (Mb) with a high affinity for the CD8 glycoprotein. The minibody is conjugated with deferoxamine (Df) and radiolabeled with the positron emitting radionuclide Zirconium-89 (89Zr). 89Zr-Df-crefmirlimab was designed to enable whole body PET imaging of CD8+ (positive) cells. We hypothesize that 89Zr-Df-crefmirlimab PET may aid the detection of inflammation in GCA and RA, given the important role of CD8+ T cells in the pathobiology of both diseases. This could potentially lead to better treatment decisions in patients with GCA and RA.

Study objective

Primary Objective: to evaluate arterial or synovial 89Zr-Df-crefmirlimab uptake on PET/CT in patients with GCA or RA

Secondary objectives are:
1. Assessment of the relationship between 89Zr-Df-crefmirlimab uptake and the presence of CD8 T cells in histological analysis of the temporal artery biopsy in patients with newly-diagnosed, cranial GCA
2. Assessment of the relationship between 89Zr-Df-crefmirlimab uptake and clinical joint assessment and histological analysis of synovial tissue in patients with RA.

Study design

Study design: A proof of concept, multicentre, prospective study.

Intervention: A single 89Zr-Df-crefmirlimab PET/CT scan will be performed in patients with GCA and RA. Synovial biopsy will be obtained from all patients with RA for research purposes only. If a temporal artery biopsy has been performed as part of standard care, patients will be asked for permission to use remaining tissue to evaluate the biopsies for the presence of CD8 T cells.

Intervention

89Zr-Df-crefmirlimab PET/CT

Study burden and risks

89Zr-Df-crefmirlimab is a radioactive compound and therefore, will cause radiation burden to the patient. The projected effective dose after receiving 18.5 ± 20% MBq (0.5 mCi) of 89Zr-Df-crefmirlimab is 12 mSv. For patients scanned with PET/CT scanners a low dose attenuation correction CT scan, which has an effective dose of 1 mSv, will be carried out. Patients will undergo a scan at injection, and at 5 hours, 1 day and 4 days after injection of 89Zr-Df-IAB22M2C, which is associated with an effective dose of 1+1+1+1 = 4 mSv. This will bring the total projected effective dose during the study to 12+4 = 16 mSv. There is a very small chance of bleeding and hematoma due to synovial biopsy in patients with RA. No direct benefits are expected for study participants. We expect no risks related to 15 mL blood withdrawal by venapunction. We aim to provide the proof of concept that the 89Zr-Df-crefmirlimab PET/CT scan might help to more accurately detect arterial and synovial inflammation in patients with GCA and RA, respectively. An adequate diagnosis and proper disease monitoring of GCA and RA are essential to prevent the development of disease complications, while minimizing unnecessary exposure to immunosuppressive treatment. We see this proof of concept study with CD8 T cell imaging by positron emission tomography with 89Zr-Df-IAB22M2C, as the way to organize a breakthrough in the field of GCA and RA diagnostics.

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

Giant cell arteritis
- Age > 50 years
- Erythrocyte sedimentation rate (ESR) >=50 mm/hr or C-reactive protein (CRP) >= 10 mg/L
- Clinical symptoms of GCA present at time of inclusion:
• Large vessel GCA (at least one of the following): constitutional symptoms (fatigue, fever, weight loss, and/or night sweats), limb claudication, or symptoms of polymyalgia rheumatica (i.e. shoulder and/or hip girdle pain associated with morning stiffness)
• Cranial GCA (at least one of the following): new-onset localized headache, scalp tenderness, temporal artery abnormality (thickening, tenderness, and/or decreased pulsation), ischemia-related vision loss, stroke, transient ischemic attack, jaw or tongue claudication (pain upon mastication).
- Imaging findings or temporal artery biopsy findings consistent with GCA at the time of inclusion
• Large vessel GCA as suggested by ultrasonography or FDG-PET/CT
• Cranial GCA as suggested by ultrasonography FDG-PET/CT or temporal artery biopsy and confirmed by temporal artery biopsy
- Patients must be able to adhere to the study appointments and other protocol requirements.
- Patients must be capable of giving informed consent and the consent must have been obtained prior to the study related procedures.

Rheumatoid arthritis
- Patients must be at least 30 years of age
- Diagnosis of rheumatoid arthritis according to the 2010 ACR/EULAR Rheumatoid Arthritis classification criteria.
- Patients with clinically active disease as assessed by a physician; with arthritis in at least one wrist, knee or ankle joint and have a clinical indication to initiate or escalate treatment
- Treatment with disease modifying anti-rheumatic drugs (DMARDS) and oral corticosteroid up to 10 mg daily is allowed, provided that there is a stable dose for at least 4 weeks prior to inclusion
- Non-steroidal anti-inflammatory drugs (NSAID) is permitted, provided that there is a stable dose for at least 4 weeks prior to inclusion
- Patients must be able to adhere to the study appointments and other protocol requirements

- Patients must be capable of giving informed consent and the consent must have been obtained prior to the study related procedures.

Exclusion criteria

Giant cell arteritis
- Age <= 50 years
- Use of oral, intravenous or intramuscular glucocorticoids within 4 weeks prior to inclusion.
- Use of disease-modifying antirheumatic drugs (DMARD) within 3 months prior to inclusion.
- Treatment with any investigational drug within 3 months prior to inclusion.
- Known pregnancy or breast feeding
- Research-related radiation exposure (cumulative >=5 mSv) in the year before inclusion.
- Urinary or faecal incontinence

Rheumatoid arthritis
A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Age < 30 years
- Use of intra-articular, intramuscular or intravenous corticosteroids within 4 weeks prior to inclusie
- Treatment with any investigational drug within the previous 3 months
- Known pregnancy or breast feeding
- Research related radiation exposure (cumulative >=5 mSv) in the year before inclusion
- Urinary or faecal incontinence

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-12-2023
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	89Zr-Df-crefmirlimab
Generic name:	89Zr-Df-crefmirlimab

Ethics review

Approved WMO Date:	22-11-2022
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-06-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
Other	2022-002822-28
EudraCT	EUCTR2022-002822-28-NL
CCMO	NL82421.042.22