[18F]fluor-PEG-folate PET/CT imaging in Giant Cell Arteritis.

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Primary Objective: to evaluate arterial [18F]fluor-PEG-folate uptake on PET/CT in patients with active, large vessel GCA; and in the same patients after 9 months of standard treatment.Secondary objectives are:- Assessment of the relationship between...

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

Summary

ID

NL-OMON52861

Source
ToetsingOnline

Brief title
Macrophage imaging GCA

Condition

- Autoimmune disorders
- Vascular disorders NEC

Synonym
giant cell arteritis, vasculitis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Horizon 2020 (Europese Unie)

Intervention

Keyword: artery, giant cell arteritis, macrophage, PET/CT

Outcome measures

Primary outcome

Our main endpoint is the visualization of inflamed arteries at baseline and

after 9 months of standard treatment.

Secondary outcome

Our secondary endpoints are the association between [18F]fluor-PEG-folate

uptake after 9 months of treatment and clinical disease activity at that time

point and the development of relapses during the first 9 months of treatment.

Study description

Background summary

Giant Cell Arteritis (GCA) is a chronic systemic inflammatory disease that primarily affects the large and medium-sized arteries. The inflammation is usually chronic, and may lead to ischemic complication due to occlusion/stenosis. A late complication is the development of aortic aneurysms. Standard treatment consists of high-dose glucocorticoids which are tapered within 1-1.5 years. Symptoms, physical signs and laboratory tests are not specific for GCA. Recent international guidelines therefore emphasize the importance of imaging as a diagnostic tool for visualizing vessel wall inflammation in GCA. Imaging might help to establish the initial diagnosis of GCA and to estimate disease activity during follow-up. An adequate diagnosis and proper disease monitoring are essential to prevent the development of complications of GCA, while minimising unnecessary exposure to immunosuppressive treatment. Currently, the fluorine-18-deoxyglucose positron assemission tomography/computer tomography (FDG-PET/CT) is used as diagnostic imaging modality in GCA. FDG-PET/CT visualises tissues with high glucose metabolism, including tissues that are inflamed. One of the drawbacks of the FDG-PET/CT is the substantial decrease in sensitivity after 3 days of glucocorticoid treatment. Another disadvantage is its reliance on glucose metabolism. This further limits FDG-PET/CT scanning in patients with poorly controlled diabetes, a known complication of glucocorticoid treatment.

Furthermore, arteries with a close relation to metabolically active organs (such as the brain) cannot be evaluated by the FDG-PET/CT scan.

An alternative approach might be to visualize specific immune cells in the arterial wall of patients with GCA. Biopsy studies indicate that macrophages could be an excellent target for such imaging studies. Recently, the novel macrophage tracer [18F]fluor-polyetyhylene glycol (PEG)-folate has been developed for PET/CT imaging by the VU Medical Center. [18F]fluor-PEG-folate binds to the β-isoform of the folate receptor (FRβ). The [18F] tracer is stable, which allows for synthesis in a central GMP laboratory from where it can be shipped to other hospitals. [18F]fluor-PEG-folate has shown an excellent ability to detect macrophages in inflamed joints, both in an animal model of inflammatory arthritis, as well as in humans with rheumatoid arthritis. Importantly, biopsy studies haver shown that FRβ-expressing macrophages are abundant in the inflamed arteries of patients with GCA .

Study objective

Primary Objective: to evaluate arterial [18F]fluor-PEG-folate uptake on PET/CT in patients with active, large vessel GCA; and in the same patients after 9 months of standard treatment.

Secondary objectives are:
- Assessment of the relationship between the [18F]fluor-PEG-folate uptake after 9 months of treatment and clinical disease activity at that time point.
- Assessment of the relationship between the [18F]fluor-PEG-folate uptake after 9 months of treatment and the development of relapses during the first 9 months of treatment.

Study design

A multicentre (UMCG and VU Medical Center), prospective cohort study.

Study burden and risks

The total radiation burden per PET-CT scan per patient will be at 6.2 mSv.

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

-Age >= 50 years.
-ESR >=50 mm/hr (by Westergren method) or CRP >= 24.5 mg/L.
-Clinical symptoms of GCA (at least one of the following): unequivocal cranial symptoms of GCA, symptoms of polymyalgia rheumatica or constitutional symptoms.
-Imaging findings consistent with GCA (at least by one of the following methods): ultrasound, FDG-PET/CT, MRA or CTA.
-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

- Clinical symptoms suggestive of 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, transients ischemic attack, jaw or tongue claudication (pain upon mastication).
- Ultrasound findings consistent with cranial GCA (e.g. halo sign in

temporal or facial artery).
- A prior positive temporal artery biopsy.
- Initiation or dose escalation of systemic glucocorticoid therapy (oral, IM, IV) in the 4 weeks prior to inclusion
- Initiation or dose escalation of disease-modifying antirheumatic drugs (DMARDs) within 3 months prior to inclusion
- Treatment with any investigational drug within 3 months prior to inclusion.
- Females with child bearing potential. Post-menopausal women with >12 months of amenorrhoea are considered to have no child bearing potential. Given the age distribution of patients with GCA, exclusion of females with child bearing potential will not lead to recruitment bias in the study.
- Research-related radiation exposure (cumulative >=5 mSv) in the year before inclusion.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2024
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]PEG-folate
Generic name:	[18F]PEG-folate

Ethics review

Approved WMO Date:	14-07-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-02-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-08-2023
Application type:	Amendment
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:	29-01-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	17-04-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-04-2024
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
EudraCT	EUCTR2020-001019-26-NL
CCMO	NL73549.042.20