Quantitative kinetic analysis of [11C]DPA-713 and [18F]PEG-Folate uptake in joints of patients with rheumatoid arthritis

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Primary Objective: Development of a tracer kinetic model for tracers [11C]DPA-713 and [18F]PEG-Folate.Secondary Objectives: 1. Development of a static imaging protocol and a validated simplified measure for quantification of uptake of tracers [11C]...

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

Summary

ID

NL-OMON45561

Source
ToetsingOnline

Brief title
[11C]DPA-713 and [18F]PEG-Folate in rheumatoid arthritis

Condition

- Autoimmune disorders
- Joint disorders

Synonym
arthritis, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: [11C]DPA-713, [18F]PEG-Folate, positron emission tomography, rheumatoid arthritis

Outcome measures

Primary outcome

Development of a tracer kinetic model for tracers [11C]DPA-713 and

[18F]PEG-Folate.

Secondary outcome

1. Development of a static imaging protocol and a validated simplified measure

for quantification of uptake of tracers [11C]DPA-713 and [18F]PEG-Folate in

arthritic joints in RA patients.

2. Comparison of the static and kinetic model, leading to simplification of

protocols for routine clinical studies.

Study description

Background summary

Rheumatoid arthritis (RA) is a chronic systemic connective tissue disease that primarily affects the synovial joints. The inflammation is usually chronic, and may cause progressive destruction of bone and cartilage, eventually leading to loss of function. Recent international guidelines stress the importance of starting effective treatment as early as possible. A new diagnostic tool for early diagnostics and therapy monitoring could greatly reduce permanent physical damage.

Positron emission tomography is a highly sensitive imaging technique that enables monitoring of disease activity and therapeutic effects. PET tracers can

be specifically target to cells or molecules of interest. The macrophage has been shown to be a promising target for both early diagnostics and therapy monitoring, because of its infiltration in synovium from the early development of RA onwards. Studies by our research group have shown that macrophage PET imaging can visualize inflammatory activity in rheumatoid arthritis (RA), even at subclinical level. The potential of PET to predict therapeutic outcome of RA treatment has also been demonstrated.

Previously, our group studied the tracer [11C]-R-PK11195, which binds to peripheral benzodiazepine receptors (TSPO) on macrophages, and has shown to successfully visualize inflammatory lesions. This tracer accumulated significantly in clinically inflamed joints when compared to healthy ones. However, the relatively high level of background binding of [11C]-(R)-PK11195 in peri-articular tissues limited detection of more subtle arthritis. This finding has stimulated development of alternative macrophage tracers for arthritis imaging that display more favourite target-to-background signals in arthritic joints.

In subsequent pre-clinical and clinical proof of concept studies, we have shown that [11C]DPA713 and [18F]PEG Folate are promising novel candidate macrophage tracers to image arthritis activity in RA. A new generation TSPO tracer, is [11C]DPA-713. Is a new generation TSPO tracer that showed higher absolute uptake in arthritic joints and higher target-to-background ratios as compared to [11C]PK11195. [18F]PEG Folate targets the *-isoform of the folate receptor (FR*), which is expressed on activated macrophages. Both pre-clinical and clinical feasibility data in RA demonstrated very low background uptake and clear targeting of arthritic joints. The collected proof of concept data did not allow selection of one tracer above the other for further development towards clinical application studies. [11C]DPA713 has an interesting profile for therapy monitoring of RA treatment as C-11 has a very short half-life (20 min) and hence a low radiation burden which allows for repetitive scanning. [18F]PEG Folate seems to be particularly suited for early diagnostics of both articular and extra-articular diseases activity of RA because of low background uptake in the whole body.

Study objective

Primary Objective: Development of a tracer kinetic model for tracers [11C]DPA-713 and [18F]PEG-Folate.

Secondary Objectives:
1. Development of a static imaging protocol and a validated simplified measure for quantification of uptake of tracers [11C]DPA-713 and [18F]PEG-Folate in arthritic joints in RA patients.
2. Comparison of the static and kinetic model, leading to simplification of protocols for routine clinical studies.

Study design

A monocenter, prospective observational study in 6 patients with active rheumatoid arthritis. [11C]DPA-713 and [18F]PEG-Folate uptake will be measured quantitatively. Accuracy of blood and plasma activity concentration, plasma metabolite measurements derived from arterial and venous samples as well as the reliability of using Image Derived Input Functions (IDIF) for quantifiction of [11C]DPA-713 and [18F]PEG-Folate kinetics will be tested. Dynamic PET and CT scanning will be performed in two separate sessions on one day, first[11C]DPA-713, and subsequently (after * 5 half-lives of C-11) [18F]PEG-Folate.

Intervention

Not applicable.

Study burden and risks

- The total radiation burden will be about 8.9 mSv, therefor staying under the limit of 10 mSv.
- Venous and arterial punction with risk of local bruises.
- Very small chance of allergic reaction to PET tracer

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

* Men and women, * 18 years of age.
* Diagnosis of rheumatoid arthritis according to the 1987 revised criteria of the American Rheumatism Association (ARA) and/or the 2010 ACR/EULAR Rheumatoid Arthritis Classification Criteria.
* Patients with obvious clinical arthritis activity assessed by a physician, in at least 1 hand, wrist of knee joints.
* Treatment with disease modifying anti-rheumatic drugs (DMARDS), biologics and oral corticosteroids up to 10 mg daily is allowed. Non-steroidal anti-inflammatory drugs (NSAID) is permitted, provided that there is a stable dose for at least 1 month.
* 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

* Use of intramuscular or intravenous corticosteroids within 4 weeks prior to screening.
* Treatment with any investigational drug within the previous 3 months.
* Pregnancy or breast-feeding
* Anemia (Hemoglobine <6.0 mmol/L)
* Renal insufficiency (GFR <30 mL/min/1.73m2)

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-05-2017
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[11C]DPA-713, [18F]PEG-Folate
Generic name:	[11C]DPA-713, [18F]PEG-Folate

Ethics review

Approved WMO Date:	21-12-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-02-2017
Application type:	First submission
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
EudraCT	EUCTR2016-004423-22-NL
CCMO	NL59690.029.16