[89Zr]Df-IAB22M2C anti-CD8 minibody PET/CT imaging to assess the in vivo distribution of CD8+ T-cells in COVID-19 patients.

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We aim to assess differences in the in vivo distribution of CD8+ T-cells in patients with proven SARS-CoV-2 presenting with lymphopenia or with normal lymphocyte counts, using [89Zr]Zr-Df-IAB22M2C PET/CT imaging. Elucidating the pathophysiology…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON49545

Source
ToetsingOnline

Brief title
PET/CT imaging to track CD8+ T-cells in COVID-19 patients.

Condition

- Viral infectious disorders
- Pulmonary vascular disorders

Synonym
COVID-19; coronavirus infection

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Radboud Translational Medicine BV, NIjmegen

Intervention

Keyword: [89Zr]Df-IAB22M2C, COVID-19, PET/CT

Outcome measures

Primary outcome

The main study parameter is the whole body in vivo biodistribution of [89Zr]Df-IAB22M2C as quantified by PET/CT. All main organs will automatically be segmented using Siemens MIWBAS. The following parameters will be calculated and reported in a descriptive fashion: SUVmean ±SD, SUVmax ±SD and SUVpeak ±SD, total organ activity (% of total measured activity). Statistical tests to assess group differences will include the non-parametric Mann-Whitney U test per organ, since normal distribution cannot be assumed. Overall distribution profiles will be tested using Chi-square test.

Secondary outcome

Secondary endpoints:

Imaging related:

1) Spatial correlation (per lung segment) with ground-glass opacities, consolidation and vascular thickening

Biomarker related:

2) Absolute and relative organ uptake of [89Zr]Df-IAB22M2C will be quantitatively correlated with concurrent levels of ferritin, D-dimer, CRP, as

obtained per routine clinical care using Spearman non-parametric correlation.

3) Absolute and relative organ uptake of [89Zr]Df-IAB22M2C will be quantitatively correlated with total lymphocyte numbers, absolute and relative numbers of CD4+ and CD8+ T-cells using Spearman non-parametric correlation, as well as descriptively correlated with flowcytometric markers (PD-1, TIM-3, Granzyme B/CD127, phenotyping (CD45RA/CCR7, or CD62L/CD28) to establish effector memory/central memory, naïve and TEMRA subsets)

Clinical outcome related:

4) Absolute and relative organ uptake of [89Zr]Df-IAB22M2C will be correlated with the following clinical parameters: (time to) eventual ICU admission, length of ICU stay (days), mechanical ventilation parameters, oxygen demand, total length of hospital stay (days).

Study description

Background summary

A subset of patients diagnosed with SARS-CoV-2 infection present with lymphopenia. The degree of lymphopenia, and in particular reduced CD8+ T-cell numbers, is strongly correlated with clinical deterioration and ICU admission. In contrast, general CD3-positive T-cell numbers or CD4+ T-cell numbers are less associated.
The underlying reasons for lymphopenia in COVID-19 is currently unclear, but several hypotheses have been put forward; 1) sequestration of CD8+ T-cells in peripheral tissues (e.g. lung) either during the effector phase of their lifespan or passively by local chemotactic signals, 2) accelerated maturation and apoptosis either induced by storm of inflammatory cytokines or direct infection or 3) resulting from decreased lymphopoiesis induced by reduced levels of stem cell factor. The lack of data on in vivo distribution of CD8+ T-cells hampers a more thorough understanding of this critical prognostic

factor.

Study objective

We aim to assess differences in the in vivo distribution of CD8+ T-cells in patients with proven SARS-CoV-2 presenting with lymphopenia or with normal lymphocyte counts, using [89Zr]Zr-Df-IAB22M2C PET/CT imaging. Elucidating the pathophysiology underlying lymphopenia at early stages of disease development would allow to rationally design targeted interventions that aim to counteract the detrimental effects of lymphopenia in COVID-19 patients.

Study design

This is a prospective, observational non-randomized pilot study in 20 patients with microbiologically proven SARS-CoV-2 infection. All patients will undergo a whole body [89Zr]Df-IAB22M2C PET/CT scan.

Study burden and risks

Toxicity tests have been performed in mice and no adverse events were seen. Previous and published clinical studies with [89Zr]Df-IAB22M2C injection showed no adverse events. The risks associated with the radiolabeled minibodies injection are in general low.
PET/CT imaging with 37 MBq [89Zr]Df-IAB22M2C imposes a radiation dose equivalent of 24 mSv to the patient. The addition of the [89Zr]Df-IAB22M2C PET/CT scan will not cause a change in risk and will still be in the risk category as defined by the International Commission on Radiation Protection. Because diagnostics and treatment are not influenced by the outcome of this study, the patient will not directly benefit from participation in this study.
For translational purposes, 10 ml EDTA blood will be drawn from an intravenous line, prior to injection of the tracer, no additional vena puncture is needed.

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

All patients must meet all of the following criteria:
1. microbiologically proven SARS-CoV-19 infection;
2. More than or equal to 18 years of age;
3. Ability to provide written informed consent.

Exclusion criteria

A patient will be excluded from participation in the trial if one or more of the following criteria are met:
1. Contra-indication for PET; pregnancy, breast-feeding, severe claustrophobia
2. Contra-indication for administration of iodine-containing contrast agents
3. Other serious illness, e.g. history of malignancies or auto-immune disorders
4. Known pre-existing lymphopenia from an unrelated other medical condition
5. Estimated creatinine clearance <= 30mL/min according to the Cockcroft-Gault formula (or local institutional standard method) OR oligo-uric patients (<400mL/24hr)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-02-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[89Zr]Df-IAB22M2C
Generic name:	Niet van toepassing

Ethics review

Approved WMO Date:	12-01-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	28-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2020-005984-29-NL
CCMO	NL76248.091.20