Imaging of Rituximab-Zirconium-89 uptake with Positron-Emission-Tomography scans in active relapsing-remitting multiple sclerosis patients: a pilot study

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We here propose a pilot immuno-PET study in active relapsing MS patients to investigate safety and sensitivity of 89Zr-rituximab in detecting CD20 positive (active) MS lesions and to assess inter-patient variability in 89Zr-rituximab biodistribition...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Autoimmune disorders
Study type	Interventional

Summary

ID

NL-OMON33247

Source
ToetsingOnline

Brief title
PET with 89Zr-labelled rituximab in MS

Condition

- Autoimmune disorders
- Demyelinating disorders

Synonym
MS, Multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Stg klinische neurowetenschappen

Intervention

Keyword: Multiple sclerosis, PET, Rituximab

Outcome measures

Primary outcome

89Zr-rituximab uptake in CD20 positive (actieve) MS lesions

Secondary outcome

Inter-patient variability in 89Zr-rituximab biodistribition.

Study description

Background summary

Recent concepts of multiple sclerosis (MS) suggest that autoimmune B cells and humoral immune mechanisms may play key roles in MS. Initial beneficial results of therapies targeting B cells in patients with autoimmune diseases have been reported. A recent phase 2 clinical trial showed that rituximab, a chimeric monoclonal antibody (mAb) against CD20, reduces disease activity in relapsing-remitting MS; patients treated with rituximab had a substantial reduction in the number of clinical relapses and contrast-enhancing lesions (CEL) on magnetic resonance imaging (MRI). However, the rapid effect of rituximab on acute disease activity suggests that the beneficial mechanism in MS is not the modulation of soluble autoantibodies. Instead, several other possible explanations for the effects of rituximab in MS have been suggested. In fact, the mechanisms underlying the effects of rituximab on disease activity in MS are unclear.

The introduction of immuno-positron emission tomography (PET), the combination of PET with mAbs, is an attractive novel option to visualize molecular interactions. In MS patients, treatment with rituximab labelled with a positron emitter has the potential for quantification of the interactions of the drug within the different compartments of the body, especially the CNS, including

active lesions.

Study objective

We here propose a pilot immuno-PET study in active relapsing MS patients to investigate safety and sensitivity of 89Zr-rituximab in detecting CD20 positive (active) MS lesions and to assess inter-patient variability in 89Zr-rituximab biodistribition and targeting of CD20 positive B cells.

Study design

Six active relapsing-remitting MS patients will receive 1000-mg intravenous infusions of rituximab on study days 1 and 15. Only the first administration will be partially labelled with the positron emitter Zirconium-89. PET scans will be performed on day 1, 3 and 6.

Intervention

1000-mg intravenous infusions of rituximab on study days 1 and 15. Only the first administration will be partially labelled with the positron emitter Zirconium-89. PET scans will be performed on day 1, 3 and 6.

Study burden and risks

Physical examination
3 x PET scan
2 x MRI
Blood samples
Adverse effects rituximab

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

Diagnosis of MS
EDSS score 0.0 to 5.0
Age between 18 and 50 years
>=1 MS attack(s) in the year prior to screening
>=1 MS attack during treatment with interferon beta or glatiramer acetate

Exclusion criteria

Previous treatment with mitoxantrone, natalizumab or any investigational drug for MS the year before screening
Any progressive form of MS
Inability to undergo MRI with gadolinium administration
Pregnancy or breast feeding

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-01-2010
Enrollment:	6
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	MabThera
Generic name:	rituximab
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	na
Generic name:	Zirconium-89

Ethics review

Approved WMO

Date:	09-12-2009
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	EUCTR2009-016580-11-NL
CCMO	NL29305.029.09