Open-label, non-randomized, positron emission tomography (PET) imaging study to evaluate a single dose of 250 MBq (6.75 mCi) ZK 6032924 (18F-FEDAA1106) for its diagnostic potential in discriminating patients with probable Alzheimerâ¤*s disease from healthy volunteers and to evaluate the radiation dosimetry of a single dose of 185 MBq (5 mCi) ZK 6032924 in healthy volunteers.

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Discrimination of probable AD patients from healthy volunteers by ZK 6032924 PET imaging as evaluated by visual analysis of the brain distribution patterns and by SUV values in probable AD patients as compared to healthy volunteers for brain imaging...

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

Summary

ID

NL-OMON33961

Source
ToetsingOnline

Brief title
PET Study with ZK6032924 in probable AD patients vs HV.

Condition

- Neurological disorders NEC

Synonym
Alzheimer's disease, primary dementia

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Bayer AG

Intervention

Keyword: Alzheimer, diagnostic, healthy volunteers, PET

Outcome measures

Primary outcome

Discrimination of probable AD patients from healthy volunteers by ZK 6032924

PET imaging as evaluated by visual analysis of the brain distribution patterns

and by SUV values in probable AD patients as compared to healthy volunteers for

brain imaging.

Secondary outcome

1.Comparison of different quantification approaches for their relative

potential to discriminate AD from healthy controls.

2.Radiation dosimetry (OLINDA) in 6 healthy volunteers based on the

biodistribution of ZK 6032924 by whole body imaging.

3.Determination of safety and tolerability of ZK 6032924**

Study description

Background summary

In the body there is a receptor called PBR (Peripheral Benzodiazepine Receptor). It is found for example in the brain, in so called microglia cells. Microglia are the brain*s inflammatory cells. When tissue is damaged these cells work as cleaners, as they carry off foreign cell fragments and bacteria. During normal conditions there are low concentrations of PBR in the microglia cell, but when the cell is activated, for example due to inflammation or nerve damage, the number of PBR increases.

It is known that the concentration of PBR in the brain of patients with Alzheimer*s disease is increased. However it is not possible to visualize PBR during living.

With PET (Positron Emission Tomography) it might be possible. Positron Emission Tomography (PET) is an imaging technique to visualize metabolism in the body by injection of a very small amount of radioactive substance. The radio-active substance we use for the study is tracer [18F]FEDAA1106 (ZK 6032924). The tracer [18F]FEDAA1106 is specially developed for measurement of PBR in the brain.

Study objective

Discrimination of probable AD patients from healthy volunteers by ZK 6032924 PET imaging as evaluated by visual analysis of the brain distribution patterns and by SUV values in probable AD patients as compared to healthy volunteers for brain imaging and determination of safety and tolerability of ZK 6032924.

Study design

Open-label, non-randomized, single administration of ZK 6032924 with PET scans to 10-15 probable Alzheimer's disease patients and 10-15 human volunteers

Intervention

A single dose of radiopharmaceutical will be administered via an indwelling venous line for brain PET imaging. aterial blood samples (during PET scan for kinetics, 3x during screening, just before the PET scan and at follow-up

visit).

Study burden and risks

4x visits to the hospital (6 hours totally)
1x MRI scan
1x PET scan
1x neurological and neuropsychological testing
3x physical examination
4x ECG
During 3 visits to the hospital laboratory tests (blood and urine samples)

Probable side effects of ZK 6032924
Discomfort during penetration of the artery by the cannula and during bloodsampling, the cannula can also cause a bruise

Contacts

Public
Bayer

Muellerstrasse 170-178
D-13342
Duitsland
Scientific
Bayer

Muellerstrasse 170-178
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Duitsland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Inclusion criteria: Healthy volunteers for brain imaging
1.Healthy volunteer for brain imaging is able to understand the information provided on purpose and conduct of the clinical study, must be capable of giving fully informed consent in writing, and has read and signed the informed consent prior to study participation.
2.Healthy males and post-menopausal females aged * 50 years (the age difference between a patient and the age-matched volunteer should not be larger than 5 years; a larger difference in age will be allowed if adherence to this rule causes significant slowing of healthy volunteer recruitment rate) and BMI within the range (19 * BMI * 30).
3.Female postmenopausal status will be determined by medical history (last spontaneous bleeding at least 1 year prior to radiotracer administration or females must have had a hysterectomy or a bilateral oophorectomy at least three months prior to radiotracer administration). In addition, females must have serum follicle-stimulating hormone (FSH) levels * 40 mIU/mL and estradiol level * 20 pg/mL.
4.MMSE score of * 28
5.CDR score of zero (0)
6.Confirmation by other neuropsychological test results that the volunteer does not show any signs of cognitive impairment or dementia (e.g. results lying within an interval of one standard deviation from the mean value, mean value and standard deviations adjusted for age and education)
7.Adequate visual and auditory acuity to complete neuropsychological testing;Inclusion criteria: Probable Alzheimer*s disease patients for brain imaging
1.Patient and designee must be able to understand the information provided on purpose and conduct of the clinical study, must be capable of giving fully informed consent in writing, and have read and signed the informed consent prior to study participation.
2.Males and postmenopausal females aged * 50 years and BMI within the range (19 * BMI * 30)
3.Female postmenopausal status will be determined by medical history (last spontaneous bleeding at least 1 year prior to radiotracer administration or females must have had a hysterectomy or a bilateral oophorectomy at least three months prior to radiotracer administration). In addition, females must have serum follicle-stimulating hormone (FSH) levels * 40 mIU/mL and estradiol level * 20 pg/mL.
4.Patient fulfills DSM-IV and NINCDS-ADRDA criteria for probable AD
5.Patient has mild to moderate dementia :
a.with a dementia score between ³ 20 on the Mini-Mental Status Examination (MMSE)
b.with a Clinical Dementia Rating score of 1 or 2 (CDR)
6.Patient has had the following further tests within the 120 days preceding radiotracer administration:
- Neurological examination
- Psychometric testing
- Brain MRI
7.Adequate visual and auditory acuity to complete psychometric testing

Exclusion criteria

Exclusion criteria: probable Alzheimer*s disease patients
1.History, physical or imaging findings of other neurological illness apart from AD such as cerebrovascular disease, inflammatory or infectious disease and other degenerative diseases and any other from of dementias different from AD (e.g. Lewy Body dementia, Fronto temporal dementia or vascular dementia)
2.Lifetime history of major affective disorder, schizophrenia, schizoaffective disorder
3.MRI brain scan findings that do not reveal changes indicative of stroke and/or generalized cerebrovascular disease (e.g., the ARWMC scale) changes limited to: a white matter lesion score of 0 or 1 or 2 and a basal ganglia score of 0 or 1);Exclusion criteria: healthy volunteers for brain imaging and probable AD patients
1.Any disease, condition, or concomitant medications that significantly compromises the function of the body systems and could result in excessive accumulation, impaired metabolism, altered excretion of the radiotracer, or might interfere with the conduct of the study or interpretation of the results.
2.History of significant occupational exposure to ionizing radiation or application of radioactive substances or ionizing radiation for the purposes of diagnosis or treatment within the last year (> 10 mSv for healthy volunteers and > 50 mSV for AD patients within one year) or application of radioactive substances or ionizing exposure to radiation during an investigation / study in the year preceding the PET scan or whose occupational exposure to radioactivity is monitored.
3.Haematological or biochemical parameters that are outside the normal range and are considered clinically significant by the investigator.
4.History of or current alcohol or drug abuse/dependence.
5.History of major allergic reactions.
6.History of epilepsy.
7.History of electroconvulsive therapy.
8.Current unstable medical condition (e.g. unstable angina, myocardial infarction or coronary revascularization in the preceding 12 months, cardiac failure, chronic renal failure, chronic hepatic disease, severe pulmonary disease, blood disorders, poorly controlled diabetes, chronic infection).
9.Criteria which in the opinion of the investigator preclude participation for scientific reasons, for reasons of compliance, or for reasons of the volunteer*s safety.
10.Subjects in whom magnetic resonance imaging (MRI) is contraindicated or receipt of any contrast material (X-ray, MRI) or radiopharmaceuticals within 48 hours or 5 half lives prior to the application of the radiotracer or if application of such a substance is planned during the observation period.
11.Receiving drug therapy with known significant action on the CNS such as NSAIDs (within 24 hours), aspirin (within 12 hours), or benzodiazepines, corticosteroids, vinpocetine, vincamine and other eburnamine derivatives, within 5 half-lives of the respective drug before radiotracer administration. The intake of typical medication of the treatment of probable AD with no evidence of interfering with the peripheral benzodiazepine receptor expression in the central nervous system, such as Donepezil or similar compounds. May be continued during the study.
12.Donation of blood within 4 weeks or plasmapheresis within 2 weeks before the radiotracer

administration.
13.Current systemic autoimmune disease or clinically relevant systemic inflammatory disease.
14.History of brain surgery, intracranial hematoma, or head trauma with permanent brain lesion.
15.Subject is in custody by order of an authority or a court of law.
16.Exclusion periods from other studies or simultaneous participation in other clinical studies or previous assignment to radiotracer administration in this study.
17.Close affiliation with the investigational site (e.g. close relative of investigator), dependent person (e.g. employee or student of investigational site).
18.Allen*s test indicative of reductions in arterial perfusion of the hand which would compromise the perfusion during arterial blood sampling
19.MRI brain scan findings that reveal changes indicative of stroke and/or generalized cerebrovascular disease, e.g., the ARMWC scale with a white matter lesion score of >2 and basial ganglia score of >1.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-11-2009
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	ZK 6032924 (18F-FEDAA1106)

Ethics review

Approved WMO Date:	30-12-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2009
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-05-2009
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	EUCTR2006-006045-14-NL
CCMO	NL23773.029.08