A Biomarker Study to Measure CSF Proteins Upon Application of an Indwelling Lumbar Catheter for 36 Hours in Subjects with Mild Cognitive Impairment or Alzheimer*s Disease

Published: 15-11-2012
Last updated: 01-05-2024

Primary ObjectiveTo investigate changes of CSF proteins over time using continuous CSF sampling for 36 hours, including but not limited to A*1/x-42, A* 1/x-40, A* 1/x-38 and A* 1/x-37 in subjects with MCI or AD. Secondary Objectives1. To investigate...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Mental impairment disorders
Study type	Observational invasive

Summary

ID

NL-OMON37828

Source
ToetsingOnline

Brief title
CSF biomarker study in patients with MCI or Alzheimer's Disease

Condition

- Mental impairment disorders

Synonym
cognitive impairment, Dementia

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Janssen Cilag International

Intervention

Keyword: Alzheimer, Biomarker, CSF

Outcome measures

Primary outcome

Difference in 36-hour course of different proteins in cerebrospinal fluid

between healthy elderly subjects and patients with Alzheimer's disease or Mild

Cognitive Impairment

Secondary outcome

- difference in 36-hour course of proteins in cerebrospinal fluid in healthy

elderly subjects, between groups with and without treatment with an

anti-inflammatory marker

- difference in 36-hour course of proteins in cerebrospinal fluid in healthy

elderly subject, between a group in which sampeling starts immediately, and a

group in which sampeling starts later

Tolerability:

o adverse events

o vital signs

o safety laboratory

Study description

Background summary

For the development of new therapies targeting Alzheimer*s Disease (AD), changes of A* and/or tau are key biomarkers in discovery and potentially in clinical trials. While in preclinical studies direct measurement in the brain is possible, this is not a routine option in clinical trials. In contrast CSF, sharing the same environment, will be the best proxy to understand changes upon therapy. When not measuring directly in the brain, at the site of the pathological changes and potential therapeutic interventions, but more distant, a potential effect will be diluted and as such less pronounced. Therefore, it is crucial to optimize and understand the technique of CSF sampling and measurement of CSF proteins, to base decisions on reliable data in phase 1, proof-of-mechanism studies, for therapies targeting A*.
In this study the changes in CSF proteins over 36 hours after lumbar introduction of a spinal catheter and the reasons for the less pronounced increase in A*1-42 as seen in the previous studies will be investigated. The analytes will include, but may not be limited to A* 1/x-42, A* 1/x-40, A* 1/x-38, and A* 1/x-37 in elderly healthy subjects and subjects with Mild Cognitive Impairment (MCI) or AD. Part A of the study, CSF sampling in elderly healthy subjects is already performed.

Study objective

Primary Objective
To investigate changes of CSF proteins over time using continuous CSF sampling for 36 hours, including but not limited to A*1/x-42, A* 1/x-40, A* 1/x-38 and A* 1/x-37 in subjects with MCI or AD.

Secondary Objectives
1. To investigate the safety and tolerability of continuous CSF sampling in subjects with MCI or AD;
2. To investigate the effects of sampling frequency on changes of CSF proteins over time using continuous CSF sampling in elderly healthy subjects; and
3. To investigate the effect of an anti-inflammatory agent (Ibuprofen) on possible changes of CSF proteins over time using continuous CSF sampling in elderly healthy subjects.

Study design

This is an open-label, randomized, biomarker study without investigational medicinal product in subjects with MCI or Alzheimer*s disease.
The study will consist of an eligibility screening examination (between 21 and 2 days prior to spinal catheter insertion), an inpatient CSF

collection/measurement period (day -1 to day 3), and a follow-up examination (approximately 7 to 14 days after removal of the catheter).
For assessment schedule see flow chart.

Study burden and risks

The risk of participation includes the possible side-effects from the spinal catheter (for example headache, low bloodpressure, nausea and dizziness) and findings during test (i.e. positive test result for hepatitis B, hepatitis C or HIV).
No serious side effects are expected.
Experience with cerebrospinal fluid sampeling in patients with Alzheimer's disease or Mild Cognitive Impairment, and de development of a biomarker platform in Alzheimer's, could contribute to a reliable evalutation of the efficacy of new drugs for the treatment of Alzheimer's disease.

Contacts

Public
Janssen Pharmaceutica N.V.

Turnhoutseweg 30
Beerse 2340
BE
Scientific
Janssen Pharmaceutica N.V.

Turnhoutseweg 30
Beerse 2340
BE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

o Diagnosis of probable or possible AD (according to NINCDS-ADRDA)
o Mini Mental State Exam score of *18 at screening
o Signed informed consent, and subjects must have signed a separate written informed consent indicating willingness to participate in Part 1 genetic testing (required), and indicate either consent or refusal for Part 2 DNA storage (optional)
o Mentally capable of understanding the implications of study participation
o For MCI subjects only: biological evidence for AD (evidenced by hippocampal atrophy on MRI, positive PIB scan or a positive AD CSF biomarker pattern based on changes on A* (decrease), t-tau and p-tau (increase)

Exclusion criteria

o Clinically significant abnormal physical- or neurological examination (including fundoscopy), vital signs or 12-lead ECG at screening.
o Has a relevant history of lower back pain or scoliosis and/or major (lumbar) back surgery (microdiscectomy is allowed).
o Relevant history of or current neurological disease other than AD/MCI (including any history of postdural puncture headache).
o History of epilepsy or fits or unexplained black-outs.
o History or family history of abnormal bleeding or of blood clotting
o History of spontaneous, prolonged or severe bleeding with unclear origin.
o Positive screen for drugs or alcohol
o Current anemia
o Allergic to local anesthetics and/or chlorhexidine.
o Inability to refrain from
- Low Molecular Weight Heparin (LMWH) treatment within 12 hours prior to spinal
- Other anticoagulant treatment (besides LMWH described above) within 1 week prior to spinal catheter insertion.
- Aspirin treatment (even low dose) within 5 days prior to spinal catheter insertion.
o At pre-check:
- Topical infection or local dermatological condition at the puncture site prior to puncture (pre-puncture Day 1).
- Clinically significant acute illness within 7 days prior to the study

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-06-2012
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	15-11-2012
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
CCMO	NL40311.029.12