A First in Human Study to Evaluate the Safety, Tolerability and Pharmacokinetics of IBC-Ab002 in Persons with Early Alzheimer's Disease

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This study has been transitioned to CTIS with ID 2024-511770-76-00 check the CTIS register for the current data. Primary* To assess safety and tolerability of IBC-Ab002 following single and multiple ascending doses in persons with early ADSecondary…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Dementia and amnestic conditions
Study type	Interventional

Summary

ID

NL-OMON56092

Source
ToetsingOnline

Brief title
IBC-01-01

Condition

- Dementia and amnestic conditions

Synonym
Alzheimer disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: ImmunoBrain Checkpoint, Inc

Source(s) of monetary or material Support: ImmunoBrain Checkpoint;Inc

Intervention

Keyword: Alzheimer, anti-PD-L1, human IgGk monoclonal antibody, immune checkpoint inhibitor

Outcome measures

Primary outcome

Assessment of safety by determining the number of subjects with any Adverse

Events (AE), Serious Adverse Events (SAE) and fatal SAE, clinical laboratory

tests, cognitive worsening and electrocardiograms; CSF cell counts, development

of new abnormalities on brain MRI (high-res T1, T2*, FLAIR) scans and the

Columbia Suicidality Rating Scale (C-SSRS)

Secondary outcome

Pharmacokinetic (PK) Parameters

IBC-Ab002 concentration in serum will be measured by a validated ELISA method:

o Serum antibody concentrations

o Area under the concentration-time curve from time zero to infinity (AUCinf)

o Area under the concentration-time curve from time zero to the time of the

last measurable sample (AUClast)

o Maximum observed concentration (Cmax)

o Time to reach maximum observed concentration (Tmax)

o Terminal elimination half-life (T1/2)

o Clearance (CL)

o Volume of distribution (Vd)

o Concentrations of IBC-Ab002 in CSF at selected time points

Serological Parameters

o Number of subjects with positive serum anti-IBC-Ab002 antibodies (i.e.

Anti-drug Antibodies-ADAs)

Study description

Background summary

Alzheimer*s disease (AD) is the most common type of neurodegenerative dementia. The greatest risk factor for AD is increasing age. Gender too is a risk factor with more women than men developing the disease. In Europe, the prevalence of AD is estimated at 5.05%. In the Netherlands, in 2019, it was estimated that about 265,000 people had dementia (mainly AD) and that that number would grow to 420,000 in 2030 and 520,000 in 2040. In association with this increase in prevalence, the healthcare costs would rise from ¤6.6 billion to ¤15.6 billion in 2040. The initial and most common presenting symptom of AD is episodic short-term memory loss with relative sparing of long-term memory. Short-term memory impairment is followed by impairment in problem-solving, judgment, executive functioning, lack of motivation and disorganization, leading to problems with multitasking and abstract thinking. Acetylcholinesterase inhibitors (AChEi), the mainstay of treatment that are approved for early AD have modest effects on symptoms of the disease and there is therefore an unmet need for new and novel treatment options . Recent clinical development programs have focused on treatments that target the pathological manifestations associated with amyloid beta or aggregated tau; however, despite the successful reduction of amyloid plaque burden in patients, only minimal meaningful effects have been observed on cognitive function. IBC-Ab002 represents a novel therapeutic approach for AD. The aim of IBC-Ab002 administration is to break age/disease related adaptive immune suppression by blocking the Programmed cell death protein 1 (PD-1)/ Programmed death-ligand 1 (PD-L1) inhibitory immune checkpoint pathway.

Study objective

This study has been transitioned to CTIS with ID 2024-511770-76-00 check the CTIS register for the current data.

Primary
* To assess safety and tolerability of IBC-Ab002 following single and multiple ascending doses in persons with early AD
Secondary
* To assess the pharmacokinetics of IBC-Ab002 following a single and multiple

ascending doses in persons with early AD
Exploratory
* To evaluate the pharmacodynamic effect of single and multiple doses of IBC-Ab002 in persons with early AD
* To support the proposed mechanism of action and biological effect of IBC-Ab002
* To evaluate initial effect of IBC-Ab002 on selected efficacy measures in persons with early AD

Study design

This is a randomized, double-blind, placebo-controlled first-in-human, Phase 1, safety, tolerability, pharmacokinetic (PK) and preliminary exploratory activity study of escalating multiple IV doses of IBC-Ab002 in persons with early Alzheimer's disease. The study will have both Single- and Multiple- Ascending Dose components.
The study will have an adaptive design and will be carried out in two parts. Part A will be comprised of a Single-Ascending-Dose (SAD) study and Part B will continue dosing of Part A subjects as a Multiple-Ascending Dose (MAD) study. Adaptive features may include 1) modification of dosage levels in Parts A and B based upon emerging PK variability and PD data, 2) the ability to add or expand cohorts at the higher dose levels based on emerging safety, PK and PD data. Part A will be preceded by a Screening Period of up to 8 weeks during which subject eligibility will be assessed.
A Study Monitoring Team (SMT) will review safety, tolerability and PK data prior to opening new dosing cohorts or initiating dosing in the multiple-dose portion of the study. The SMT will meet at specified intervals to monitor study progress, and, in particular, the emerging safety and tolerability profile of IBC-Ab002. The SMT will consist at least of the Study Director, the Study Principal Investigator, the Study Statistician, Pharmacometrician, Medical Monitor and an Oncologist experienced in checkpoint inhibitor clinical trials.
Subjects in five (5) sequential cohorts of 8 subjects each will be assigned in a 3:1 ratio to receive either IBC-Ab002 or matching placebo four (4) times. Part A will be a single-ascending dose study and Part B will be a multiple ascending dose study. The two parts of the study will be intercalated such that subjects will be dosed once every 12 weeks. However, repeated dosing at any dose level will not begin until the anticipated cumulative dose for that cohort has been equaled or exceeded in Part A and/or B of the study, and appropriate safety review of data from all preceding doses in prior subjects has taken place. All subjects randomized into Part A of the study will automatically continue into Part B unless dosing is halted at the individual or group level due to safety or other concerns.

Intervention

IBC-Ab002/placebo will be administered IV. Each subjects will receive 4 dosages of the study drug or placebo throughout the study with an interval of 12 weeks

between doses.
The assigned doses for the five study cohorts will be as follows:
Cohort #1: IBC-Ab002 1 mg/kg or placebo - Single dose (Part A) and then 3 doses Q12W (Part B)
Cohort #2: IBC-Ab002 3 mg/kg or placebo - Single dose (Part A) and then 3 doses Q12W (Part B)
Cohort #3: IBC-Ab002 7 mg/kg or placebo - Single dose (Part A) and then 3 doses Q12W (Part B)
Cohort #4: IBC-Ab002 15 mg/kg or placebo - Single dose (Part A) and then 3 doses Q12W (Part B)
Cohort #5: IBC-Ab002 30 mg/kg or placebo - Single dose (Part A) and then 3 doses Q12W (Part B)

Study drug will be infused over a period of 2 hours. Study drug administration in Part A of the study may be prolonged by up to 15 minutes but should not be less than 2 hours in duration. For Part B of the study, should safety and tolerability allow, the infusion rate may be shortened to 1 hour. This decision will be at the discretion of the Study Monitoring Team (SMT) and will only be considered after all subjects have received their Part A dosing. Infusion rates may be slowed, or individual infusions may be interrupted for up to * hour, at the discretion of the Investigator in the event that infusion reactions are observed, in keeping with local protocols. Subjects assigned to receive placebo will be administered 100 mL of normal saline

Study burden and risks

it is not possible to predict all of the risks and side effects that might happen if you are given IBC-Ab002. However, humans who have taken investigational medications called *Immune Checkpoint Inhibitors* that work in a similar manner to IBC-Ab002 for the treatment of cancer have had certain side effects, which may include certain immune-related disorders. Since IBC-Ab002 is dosed only once every 12 weeks, instead of once every 2 or 3 weeks as Immune Checkpoint Inhibitors are dosed for treatment of cancer, it may be that the pattern and kind of side effects you could experience may be different.

Data on potential effects of IBC Ab002 on male and female fertility and the potential for IBC-Ab002 administration to cause fetal abnormalities receiving IBC Ab002 is unknown at this time.

Immune Checkpoint Inhibitors, which work in a similar way to IBC-Ab002 are considered immunostimulants (stimulating an immune response) and may potentially enhance the response to vaccines such as the influenza vaccine. However, there is no evidence to suggest that such an enhanced immune response can lead to a serious over stimulation of the immune system.

As with taking any medication, there is a risk of allergic reaction. If you have a very serious allergic reaction, you may be at risk of death. The study

staff are trained to recognise the symptoms and take any necessary action during the infusion to treat a serious allergic reaction.

You should not expect any clinical benefit from being in the study. It is possible that you may get better, stay the same, or get worse. The intention of this study is to determine how the study medication works and how safe it is. If you take part in this study, the results of the study will be used for further development of treatments for AD and other people with AD may be helped in case it is determined that the treatment will be safe and effective.

Contacts

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age range: 50-80 years of age at the Screening visit

2. Diagnosis of early AD based on the NIA-AA Research Framework criteria, regardless of APOE gene status
a. Biomarker classification A+T+N+ or A+T+N- based upon Screening CSF profile consistent with AD defined by either of the following criteria:
i. CSF Aβ42 < 1000 pg/mL and pTau181 > 19 pg/mL
ii. CSF pTau181/Aβ42 ratio > 0.020
b. AD Clinical Stage 3 or 4 based on the National Institute on Aging and Alzheimer's Association (NIA-AA) Research Framework criteria
i. Gradual and progressive change in memory function reported by the participant or informant for >=6 months
ii. Have a Mini-Mental State Examination (MMSE) score at Screening between 20-28 inclusive
iii. Clinical Dementia Rating Scale (CDR) global score at Screening of 0.5 or 1 with memory box score >= 0.5
3. Able to speak, read and write the local language fluently
4. With respect to symptomatic treatment for Alzheimer*s disease, subjects should either be:
a. Not treated with any approved treatments for AD with a reasonable expectation that, based on the course of illness, need for treatment is not imminent and the patient should not be initiated on treatment for the length of the study, OR
b. Stabilized on an approved medication(s) other than anti-Ab antibodies for the treatment of AD for at least 3 months prior to Baseline. The dose of the AD treatment should remain the same after entering the study
5. Subject has a study partner who spends at least 10 hours/week with the patient, and can attend all visits with the patient, report accurately on the subject*s status and ensure compliance with all study requirements

Exclusion criteria

1. Females who are not postmenopausal at Screening as defined by amenorrhea for at least 12 consecutive months or who have not been sterilized surgically (i.e. bilateral tubal ligation, total hysterectomy, or bilateral oophorectomy, all with surgery at least 1 month before Screening)
2. Males who are fertile but refuse to practice double-barrier methods of contraception with female partners of childbearing potential
3. Other than AD, neurologic or medical disorder which may impair cognition including: head trauma, seizure disorder, neurodegenerative disease, hydrocephalus, cerebral / spinal hematoma, inflammatory disease, CNS infection (e.g. encephalitis or meningitis), neoplasm, toxic exposure, metabolic disorder (including hypoxic or hypoglycemic episodes), or endocrine disorder, or any significant medical conditions that, in the opinion of the Investigator, would prohibit their participation in the study
4. As assessed by the central MRI reader,
a. Magnetic Resonance Imaging (MRI) evidence of a) more than three lacunar

infarcts, b) territorial infarct or macroscopic hemorrhage, or c) deep white matter lesions corresponding to a Fazekas score = 3
b. Presence of any structural lesion that could potentially explain the subject*s cognitive impairment, or place the subject at risk for AEs during the trial. Examples include but are not limited to: cerebral contusion, encephalomalacia, aneurysm or vascular malformation, infective lesion, intraparenchymal tumor, meningioma or arachnoid cyst larger than 1 cm in longest diameter
c. More than 5 Amyloid-Related Imaging Abnormalities-Hemorrhages (ARIA-H) (including microbleeds and areas of leptomeningeal hemosiderosis (LH)) or more than 3 areas of LH
5. Any contra-indication to undergo MRI, as judged by local PI or radiologist, including but not limited to presence of pacemaker, aneurysm clips, artificial heart valves, ear implants, ventriculoperitoneal shunt, foreign metal objects in the eyes, skin or body or any other circumstance which would contraindicate an MRI scan or impair MRI image quality, or history of claustrophobia or of not tolerating MRI scanning procedures

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	30-01-2024
Enrollment:	6
Type:	Actual

Medical products/devices used

Registration:	No

Product type:	Medicine
Brand name:	-
Generic name:	-

Ethics review

Approved WMO Date:	08-03-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	27-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EU-CTR	CTIS2024-511770-76-00
EudraCT	EUCTR2021-006580-19-NL
ClinicalTrials.gov	NCT05551741
CCMO	NL78640.056.22