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A study of t04 in subjects with Alzheimer's disease

Submission date	Recruitment status	[_] Prospectively registered
20/01/2023	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/01/2023	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
15/07/2025	Nervous System Diseases	[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Alzheimer's disease (AD) is the most common neurodegenerative disorder in the world. The aggregation of both amyloid beta (Aβ) peptides extracellularly and Tau proteins intracellularly plays key roles in the pathological consequences of AD, which lead to cholinergic neurodegeneration and eventually death. Currently, there are no effective methods to stop the progression of AD. This study aims to investigate the functional effects of t04 on AD patients. One general possible molecular mechanism underlying the effect of t04 in the treatment of AD could be that the administered t04 rapidly passes through the BBB to reach the site of injury in AD. In these sites, t04 binds to local Aβ and other detrimental proteins (including aggregated proteins, denatured proteins and other conformationally abnormal proteins), such as fibrin, probably also colocalizes with plasminogen activator system, particularly tissue-type PA (tPA), that are locally expressed upon injury; hence, these PAs convert t04 and thus gets converted into active plasmin. Active products quickly degrades Aβ, fibrin and other detrimental proteins and cleaves nearby pro-BDNF or pro-NGF to generate their mature forms, which exert neuroprotective effects on damaged cholinergic neurons to promote their regeneration in the hippocampus and other areas. In addition, t04 further enters neurons to directly degrade the hyperphosphorylated intraneuronal Tau protein or indirectly improve its degradation by interacting with the autophagy-lysosome pathway (ALP) and the ubiquitin-proteasome system (UPS). All these mechanisms contribute to the alleviation of neurodegeneration and eventually lead to cholinergic neuron regeneration and improvements in memory function in AD model mice and human patients.

Who can participate?
Patients with AD

What does the study involve?
This is an open-label, one-arm, non-randomized study. t04 is given to patients with AD for a treatment duration of 72 weeks.

What are the possible benefits and risks of participating?
Patients can get free medication, and through participation in this study, the memory function of the patients will be improved after t04. Considering the properties of t04, there may be the risk of bleeding, hypersensitivity Reactions and infection after receiving a t04 injection.

Where is the study run from?
Based on the condition of the patients, the intervention was performed at the home of patients or at Beijing Chang'an Chinese and Western Integrated Medicine Hospital.

When is the study starting and how long is it expected to run for?
August 2018 to September 2021

Who is funding the study?
Talengen Institute of Life Sciences (China)

Who is the main contact?
Ms Chunying Guo, guocy@talengen-pharma.com

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Protocol serial number
CA-18-09

Study information

Scientific Title
A study of t04 in subjects with Alzheimer’s disease

Study objectives
t04 alleviates neurodegeneration and leads to cholinergic neuron regeneration and improvements in memory function in human patients with Alzheimer’s disease

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/09/2018, The Ethics Committee of Beijing Chang’an Chinese and Western Integrated Medicine Hospital (19 Zaolinqian St, Xicheng District, Beijing, China; +86-13522667371; 421337949@qq.com), ref: none provided

Primary study design
Interventional

Study design
Prospective interventional study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Alzheimer’s disease

Interventions
In this study, a treatment called t04 was given to patients with Alzheimer's disease. The treatment was given by clinical doctors or nursing staff with more than 5 years of experience and was administered face-to-face, either at the patient's home or at a hospital in Beijing. The study was open-label, meaning that everyone involved knew what treatment was being given, and it was not a randomized study. The treatment was given for 72 weeks using an intravenous injection at a dose of 50-200 mg, given 1-3 times a day. Sometimes, an atomization inhalation treatment was also used alongside the injection. The effectiveness of the treatment was measured by trained evaluators who assessed the patient's memory function using the Minimum Mental State Examination (MMSE).

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Plasminogen

Primary outcome(s)
Memory function measured using the Minimum Mental State Examination (MMSE) test at baseline and 2, 6, 10, 22 and 46 weeks

Key secondary outcome(s)
Adverse events measured using blood routine tests, blood biochemistry, coagulation function, hemolysis function, routine urine test, 12 lead ECG, physical examination, and vital signs, etc at baseline and 22 and 46 weeks

Completion date
01/09/2021

Eligibility

Key inclusion criteria
1. Written informed consent/assent obtained prior to any assessment performed
2. Age 50 to 100 years old (including 50 and 100 years old), male or female
3. Meet the diagnostic criteria of "likely ad dementia" of the National Institute on aging Alzheimer's disease association (NIA-AA) (2011)
4. The subjects are primary school graduates/graduates and above, and have the ability to complete the cognitive ability test and other tests specified in the program
5. Memory loss lasted for at least 6 months and tended to worsen gradually
6. Subjects with mild or moderate illness: 0 ≤ total score of MMSE ≤ 26
7. Total score of Clinical Dementia Rating Scale (CDR): Mild dementia: CDR = 1.0; Moderate dementia: CDR = 2.0

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
50 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
6

Key exclusion criteria
1. Dementia caused by other reasons: vascular dementia, central nervous system infection, Creutzfeldt Jakob disease, Huntington's disease, Parkinson's disease, Lewy body dementia, traumatic dementia, other physical and chemical factors (such as drug poisoning, alcoholism, carbon monoxide poisoning, etc.), important physical diseases (such as hepatic encephalopathy, pulmonary encephalopathy, etc.), intracranial space occupying lesions (such as subdural hematoma, brain tumor), endocrine disorders (such as thyroid disease, parathyroid disease), and vitamin B12, folic acid deficiency or any other known cause;
2. Have suffered from central nervous system diseases (including stroke, optic neuromyelitis, epilepsy, etc.);
3. Subjects who were diagnosed with psychiatric disorders according to DSM-V criteria, including schizophrenia or other mental diseases, bipolar disorder, severe depression or delirium;
4. Abnormal laboratory indexes: liver function (ALT and AST) exceeded 1.5×ULN, renal function (CR) exceeded 1.5×ULN, and creatine kinase exceeded 2×ULN;
5. Untreated hypertensive and hypotensive subjects at screening, or hypertensive subjects with uncontrolled hypertension after treatment; subjects with good blood pressure control after treatment can be determined by the investigator to be suitable for inclusion in this study;
6. Within 1 month of the screening visit, the subject has new or ongoing unstable or serious heart, lung, liver, kidney and hematopoietic diseases according to the judgment of the researcher, and does not meet the conditions for clinical research;
7. Clinically, people with significant allergic reaction history, especially drug allergy history, or known allergy to this product and its excipients;
8. Dyspepsia, esophageal reflux, gastric bleeding or peptic ulcer disease, frequent heartburn (≥ once a week) or any surgical operation that may affect drug absorption (such as partial/total gastrectomy, partial/total small bowel resection and cholecystectomy) within 6 months before screening
9. Alcohol or drug abusers
10. Human immunodeficiency virus antibody (ant HIV) and Treponema pallidum antibody (ant TP) are positive
11. Those who are currently using and cannot stop using drugs for Alzheimer's disease
12. Female subjects with positive pregnancy test or lactation and subjects unable to take

effective contraceptive measures or have family planning
13. Participated in other clinical trials within 3 months before the screening visit
14. There are other situations that the researcher believes are not suitable for participation in this study

Date of first enrolment
05/10/2018

Date of final enrolment
05/10/2020

Locations

Countries of recruitment
China

Study participating centre
Beijing Chang'an Chinese and Western Integrated Medicine Hospital
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Sponsor information

Organisation
Talengen Institute of Life Sciences

Funder(s)

Funder type
Research organisation

Funder Name
Talengen Institute of Life Sciences

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Ms Chunying Guo, guocy@talengen-pharma.com.

The type of data that will be shared comprises a table showing the scoring records, clinical observation record forms, images, videotapes, and detection data. Dates of availability: 05/10 /2023 to 05/10/2033.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file			27/01/2023	No	No