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Imaging-based Thrombolysis trial in Acute Ischemic Stroke-II

Submission date	Recruitment status	[_] Prospectively registered
14/10/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
30/10/2007	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
30/10/2012	Circulatory System	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
6

Study information

Scientific Title

Acronym
ITAIS-II

Study objectives
To extend the time window for thrombolysis with recombinant tissue Plasminogen Activator (rtPA) in acute ischemic stroke patients, the most significant imaging for selecting patients to implement rt-PA thrombolysis is multi-Computerised Tomography (CT) which includes Non-Enhanced CT (NECT), Computed Tomography Angiography (CTA) and CT Perfusion (CTP), or multi-MR which includes Magnetic Resonance Angiography (MRA), Diffusion-Weighted Imaging (DWI) and Perfusion-Weighted Imaging (PWI). But CT is not only more universal but also cheaper and time-saving than MR. The objective of this trail is to investigate:
1. For the selected acute ischemic stroke patients with CTP/CTA-Source Images (CTA-SI) mismatch in 3-9 hr time-window, whether the efficacy and safety of IntraVenous (IV) thrombolysis are equivalent with the routine and the classical National Institute of Neurological Disorders and Stroke (NINDS) trial which were in 3 hr time-window
2. Whether m-CT in super-early stage of stroke can predict the outcome of the patient and the efficacy of thrombolysis
3. Whether the improvement of m-CT imaging can be a substitutive indication to evaluate the outcome, and whether there is a significant correlation between the improvement and the clinical outcome

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approval gained from the Beijing Tiantan Hospital Capital Medical University Ethics Board on October 10, 2006.

Study design
A prospective, multi-center, assessor-blind controlled study.

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute ischemic stroke

Interventions
In all trial centers, consecutive acute ischemic stroke patients within 9 hr time-window will be screened, and those within 3-9 hr time-window must undergo mCT examination. All patients who meet the inclusion criteria will be included in this trial and will be treated by rt-PA 0.9 mg/kg (IV) thrombolysis. 10% of the total dose will be given as a bolus in 1 minute, and the remaining will be given as an infusion over 1 hr. All participants will be divided into 3hr time-window group and 3-9 hr time-window group.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Recombinant tissue Plasminogen Activator (rtPA)

Primary outcome(s)
1. Reperfusion improvement was assessed 24 to 48 hours post-treatment and defined as either greater than or equal to 30% reduction of Mean Transit Time (MTT) volume of abnormality or greater than or equal to 2 points improvement on the TICI grading scheme
2. Good clinical outcome at 90 days defined as a modified Rankin Score (mRS) of 0-1
3. Intracerebral haemorrhage within 24-36 h after thrombolysis

Key secondary outcome(s))
Proportion of participants who achieve the following:
1. mRS 0 to 2 at 90 days
2. Barthel Index (BI) score of 75 to 100 at 90 days
3. NIHSS 4 points improvement or 0-1 at 2 hours after treatment
4. NIHSS 4 points improvement or 0-1 at 24 to 48 hours
5. NIHSS 4 points improvement or 0-1 at day 7

Completion date
01/06/2010

Eligibility

Key inclusion criteria
For patients within 3 hrs time-windows, the only inclusion criterion for rt-PA (IV) thrombolysis is to satisfy the product instruction of rt-PA. The following are the inclusion criteria for patients within 3-9 hrs time-windows:
1. Female or male inpatients
2. Age 18-80 years
3. Clinical diagnosis of ischaemic stroke
4. Onset of symptoms within 3-9 hours prior to initiation of thrombolysis treatment
5. Stroke symptoms present for at least 30 minutes and has not significantly improved before treatment
6. The National Institute of Health Stroke Scale (NIHSS) score of greater or equal to 4
7. m-CT screening to be started within 8.5 hrs after stroke onset
8. Perfusion abnormality of CT scan >2cm in diameter involving hemisphere
9. CT perfusion/CTA source image mismatch greater than or equal to 20%
10. CTA shows occlusion or significant stenosis of large vessels (Thrombolysis in Cerebral Ischemia [TICI] grade is 0 or 1)
11. Patients are willing to receive thrombolysis treatment and to give informed consent
12. Patients are willing and able to comply with the study protocol

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
80 years

Sex
All

Key exclusion criteria
For patients within 3 hrs time-windows, the only exclusion criterion for rt-PA (IV) thrombolysis is to satisfy the product instruction of rt-PA. The following are the exclusion criteria for patients within 3-9 hrs time-windows:
1. Evidence of IntraCranial Haemorrhage (ICH), brain tumors, vascular malformation, aneurysm, SubArachnoid Hemorrhage (SAH)
2. Major infarct involving >1/3 of MCA territory on the CTA-SI
3. Presenting obvious neurologic deficits because of past stroke (modified Rankin Scale [mRS] >2)
4. Severe stroke as assessed clinically (e.g. NIHSS >25) and/or by appropriate, magnetic imaging techniques
5. Seizure at onset of stroke
6. Prior stroke within the last 3 months
7. Patients with any history of prior stroke and concomitant diabetes
8. Administration of heparin within the previous 48 hours and a thromboplastin time exceeding the upper limit of normal for laboratory
9. Platelet count of below 100,000/mm3.
10. Uncompensated hypertension at study entry or hypertension requiring aggressive treatment to reduce blood pressure to nonhypertensive limits. Uncompensated hypertension is defined as systolic blood pressure >185 mm Hg or diastolic blood pressure >=110 mm Hg on 3 repeated measures at least 10 minutes apart
11. Blood glucose <50 or >400 mg/dl
12. Known haemorrhagic diathesis within the last 6 months
13. Patients receiving oral anticoagulants, e.g. warfarin sodium, and coagulant response time (INR) >1.5
14. Known history of or suspected intracranial haemorrhage including subarachnoid haemorrhage
15. Pregnancy or lactation
16. Any history of severe central nervous system damage (i.e. neoplasm, aneurysm, intracranial or spinal surgery)
17. Haemorrhagic retinopathy,e.g. in diabetes (vision disturbances may indicate haemorrhagic retinopathy)
18. Bacterial endocarditis, pericarditis
19. Prolonged traumatic external heart massage, or recent (less than 10 days) obstetrical delivery or recent puncture of a non-compressible blood-vessel (e.g. subclavian or jugular vein puncture)
20. Acute pancreatitis
21. Documented ulcerative gastrointestinal disease during the last 3 months
22. Oesophageal varices, arterial aneurysm, arterial/venous malformation

23. Neoplasm with increased bleeding risk
24. Severe liver disease, including hepatic failure, cirrhosis, portal hypertension, oesophageal varices and active hepatitis
25. Major surgery or significant trauma in past 10 days
26. Known serious sensitivity to alteplase

Date of first enrolment
01/10/2007

Date of final enrolment
01/06/2010

Locations

Countries of recruitment
China

Study participating centre
Neurology Department
Beijing
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100050

Sponsor information

Organisation
Beijing Tiantan Hospital (China)

ROR
https://ror.org/003regz62

Funder(s)

Funder type
Government

Funder Name
The Ministry of Science and Technology and the Ministry of Health of the People's Republic of China - the key scientific research program of the 11th National Five-Year Planning of China

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2009		Yes	No