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Imaging-based Thrombolysis Trial in Acute Ischemic Stroke

Submission date	Recruitment status	[ ] Prospectively registered
18/11/2005	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
05/12/2005	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/09/2009	Circulatory System	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof Yongjun Wang

Contact details
No.6
Tiantanxili
Chongwen District
Beijing
China
100050
+86 (0)10 67038316
yongjunwang111@yahoo.com.cn

Additional identifiers

Protocol serial number
2004BA714B6

Study information

Scientific Title

Acronym
ITAIS

Study objectives
Thrombolysis with recombinant tissue plasminogen activator (rt-PA) is an effective therapy for ischemic stroke within 3 hours, but most acute ischemic stroke patients arrive at hospital after the 3-hour time window. To select patients by modern magnetic resonance imaging (MRI) technology may extend this time window. Mismatch between perfusion weighted image (PWI) deficits and diffusion weighted image (DWI) lesions putatively represents the penumbra. Intra-arterial thrombolysis is also a promising therapy for those patients beyond the 3-hour time window. And until now, there is still no strict randomized controlled trial to compare safety and efficacy between intravenous and intra-arterial thrombolysis with rt-PA.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The protocol has been approved by the Institutional Review Board of the Beijing Tiantan Hospital and other hospitals.

Study design
Prospective multicentre randomised open (assessor-blind) trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
This is a prospective, multicenter, randomized, open, assessor-blind study to assess the efficacy and safety of intra-arterial and intravenous thrombolysis in acute ischemic stroke patients within 3-9 hours time window to use MRI both for patient selection and as a primary efficacy endpoint.

Patients in 3-6 hours time window receive intra-arterial or intravenous thrombolysis with rt-PA randomly. Patients in 6-9 hours time window receive intravenous thrombolysis or conventional therapy randomly. All enrolled patients have standardized DWI, PWI and MRA.

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
1. Imaging outcome:
a. Reperfusion was assessed 24 to 48 hours posttreatment and defined as either >=30% reduction of mean transit time (MTT) volume of abnormality or >=2 points improvement on the

TICI grading scheme using MRA
b. The change in infarct lesion volume on DWI from baseline to 24 to 48 hours and 21 days

2. Clinical outcome:
a. Global outcome at day 90:
The combined analysis of the NIHSS, modified Rankin scale (mRS), and Barthel Index (BI) defined as ≥8 points improvement or scoring 0 to 1 on the NIHSS, a score of 0 to 2 on mRS, and a BI score of 75 to 100.
Modified Rankin Scale 0-1, Barthel Index ≥95, NIHSS 0-1 (inclusive distal motor function)
b. Disability status at day 90:
mRS 0-2 (independent outcome), Barthel Index >=85

Key secondary outcome(s)
1. Functional status at day 30:
mRS (total score), median Barthel Index (total score), median NIHSS (total score), mean/median change from baseline NIHSS (8 points improvement or 0-1)
2. Functional status at day 7:
NIHSS (total score), mean/median change from baseline NIHSS (4 points improvement or 0-1)
3. Functional status at 24 to 48 hours:
NIHSS (total score), mean/median change from baseline
4. Functional status at day 0 (1 and 2 hours after treatment):
NIHSS (total score), mean/median change from baseline
5. Stratified endpoint of NIHSS and mRS:
NIHSS <8: mRS 0 response,
8<=NIHSS<=14: mRS 0-1 response, NIHSS >14: mRS 0-2 response
6. Length of stay in hospital

Completion date
01/06/2007

Eligibility

Key inclusion criteria
1. Age 18-75 years
2. Clinical signs consistent with the diagnosis of ischemic stroke
3. Treatment onset within 3-9 hours after stroke onset
4. No prior neurologic event that would obscure the interpretation of the signal
and current presenting neurologic deficits (modified Rankin scale [mRS] ≤1)
5. National Institutes of Health-Stroke-Scale (NIHSS) score >4 and at least moderate limb weakness
6. MRI screening to be started within 7.5 hours after stroke onset
7. Perfusion abnormality of >2 cm in diameter involving hemispheric gray matter
8. Perfusion/diffusion mismatch of ≥20
9. Magnetic resonance angiography (MRA) shows that TICI grade is 0 or 1

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Key exclusion criteria
1. Patients not eligible to receive trial treatment within 30-60 min after completion of MRI1
2. Coma
3. Stroke symptoms are rapidly improving by the time of randomization
4. Major stroke symptoms (>25 to 30 on the NIHSS)
5. History of stroke within the previous 6 weeks
6. Seizure at the onset of stroke
7. Stroke due to a neurointerventional procedure for treatment of a cerebral aneurysm and/or cerebral arteriovenous malformation (stroke due to diagnostic cerebral angiography or cardiac catheterization might be treated)
8. Clinical presentation suggestive of subarachnoid hemorrhage, even when the MRI is normal
9. History of intracerebral hemorrhage (ICH) at any time, neoplasm, subarachnoid hemorrhage (SAH), arteriovenous malformation (AVM) or aneurysm
10. Presumed septic embolus
11. Presumed pericarditis related to recent acute myocardial infarction
12. Recent (within 10 to 30 days) surgery, biopsy of a parenchymal organ, or lumbar puncture
13. Recent (within 10 to 30 days) trauma (including head trauma), with internal injuries or ulcerative wounds
14. Known active inflammatory bowel disease, ulcerative colitis, or diverticular disease
15. Any active or recent (within 10 to 30 days) hemorrhage
16. Known hereditary or acquired hemorrhagic diathesis. Baseline laboratory values that reveal platelets are <100 000/µl, hematocrit or platelet cell volume <25 volume %, or oral anticoagulant therapy with an international normalized ratio >1.7.
17. Pregnancy, lactation, or parturition within the previous 30 days
18. Known serious sensitivity to radiographic contrast agents
19. Other serious, advanced, or terminal illness such that life expectancy is <1 year
20. Any other condition that the physician believes would pose a significant hazard to the patient if fibrinolytic therapy were initiated (e.g. amyloid angiopathy)
21. 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 >180 mmHg or diastolic blood pressure ≥105 mmHg on 3 repeated measures at least 10 minutes apart. Aggressive treatment is defined as the need for a continuous, parenteral antihypertensive, such as a nitroprusside drip, or the need to administer >3 doses of a parenteral antihypertensive, such as labetalol or Urapidil.
22. Evidence of ICH or SAH
23. DWI abnormality involving >1/3 of middle cerebral artery (MCA) territory
24. No perfusion deficit

25. Any intracranial pathology interfering with the assessment of diffusion and perfusion abnormalities
26. Contraindications to MRI

Date of first enrolment
01/06/2005

Date of final enrolment
01/06/2007

Locations

Countries of recruitment
China

Study participating centre
No.6
Beijing
China
100050

Sponsor information

Organisation
Ministry of Science and Technology of the People's Republic of China (China)

ROR
https://ror.org/027s68j25

Funder(s)

Funder type
Government

Funder Name
th Five-year National Key Technologies R&D Program (ref: 2004BA714B6)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration