Detailed NEST-3 Inclusion and Exclusion Criteria

Inclusion details

1. The subject is at least 40 years of age at screening, but has not had their 81st birthday.
2. Clinical diagnosis of acute ischemic stroke
3. Subject is not a candidate for treatment with neurothrombectomy based on the opinion of the investigator or on subject refusal.
4. Initiation of the TLT procedure begins between 4.5 and 24 hours of the time of stroke onset. The time of stroke onset is defined as the time at which a change in the baseline neurological function occurred. If the time is not known (e.g., the subject awakens from sleep with new symptoms), the last time the subject was observed by another individual to be neurologically intact must be considered to be the time of onset.
5. Baseline NIHSS score of >7 and <17 just prior to randomization
6. Full functional independence just prior to the present stroke episode as defined by the following criteria:
    a. Estimated pre-stroke mRS score less than 2
    b. Ambulates independently, may need a cane or walker, but does not need the assistance of another person
    c. Absence of a medical/physical/mental condition that substantially limits the subject's ability to work, study, participate in leisure activities, or look after family at home
    d. Completely independent, does not need supervision (may live with other individuals, but could live alone if necessary)
7. Negative pregnancy test in females of childbearing potential
8. Subject Informed Consent obtained in writing in compliance with local regulations prior to enrollment into this study.
9. The subject (and caregiver, if applicable) is willing to participate in this study for at least 90 days after the onset of stroke.

Exclusion Criteria:

1. Evidence on a CT or appropriate MRI imaging sequence of:
    An intracranial, subdural, or subarachnoid hemorrhage
        Or
    Clinical presentation suggestive of subarachnoid hemorrhage even if the initial CT/MRI scan is normal (*A scan showing HI I, defined as small petechiae along the margins of the infarct, is not a reason for exclusion provided the diagnosis is acute ischemic stroke.)*
2. Acute ischemic strokes located exclusively in the brainstem, or cerebellum, or massive hemispheric strokes (including massive bilateral strokes) are excluded if noted on clinical examination or definitively via imaging (e.g. evidence on a CT or appropriate MRI imaging sequence of a brainstem or cerebellar stroke, small deep infarction, or obvious hypodensity on CT with >1/3 MCA territory involvement)
3. A rapidly improving neurological status that, in the opinion of the Investigator, suggests that the subject is experiencing a transient ischemic attack (TIA)
4. The subject had a seizure at stroke onset or within the 7 days prior to stroke onset.
5. Sustained blood glucose >300 or <60 mg/dl (>16.7 or <3.3 mmol/l)

6. Sustained hypertension (SBP >220 mmHg or DBP >140 mmHg) or a need for aggressive repeated treatment to reduce blood pressure during the baseline period (necessity of repeated Nitroprusside or other aggressive antihypertensive therapy)
7. Sustained hypotension (SBP <80 mmHg or DBP <50 mmHg) or the need for repeated treatment to elevate blood pressure during the baseline period
8. A presumed and/or confirmed septic embolus
9. The subject has a history of CNS vascular disease (e.g. aneurysm, AVM).
10. The subject has a history of CNS disease or damage (e.g. neoplasm or dementia) which may influence the subject's outcome assessment.
11. The subject has an implant of any kind in the head (e.g. stent, clipped aneurysm, embolised AVM, implantable shunt – Hakim valve).
12. The subject has a significant skin condition (i.e., hemangioma, scleroderma, psoriasis, rash, open wound or tattoo) on their scalp that is found to be directly below three or more TLT procedure sites.
13. Use of any intravenous or intra-arterial thrombolytic medication or any investigational product (drug or device) for the treatment of this stroke episode.
14. The subject has undergone any diagnostic or therapeutic interventional neurovascular procedure, including mechanical recanalization, whether successful or unsuccessful, during this stroke episode.
15. The subject previously participated in another Phase I, II, or III investigational drug or any device trial within the preceding four weeks.
16. The subject is a female who is pregnant or lactating (within the previous 30 days), or who is of childbearing potential unless she is surgically sterile or she and/or her partner are using a medically acceptable method of birth control.
17. Any use of light-activated drugs (photodynamic therapy) within14 days prior to study enrollment
18. The subject participated in either the NEST-1 or NEST-2 Study.
19. The subject has any co-existing or terminal disease that may limit life expectancy or any medical condition (e.g. morbid obesity, substance abuse) that may, in the clinical judgment of the Investigator, independently influence the subject's outcome during the course of the study.
20. The subject is otherwise determined, based on the opinion of the Investigator, to be an unsuitable candidate for enrollment in this study.

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