StrokeNet

Clinical Trial Feasibility:

Population-Based Medical Eligibility Assessment

Title of Proposal: DEFUSE

PI: Greg Albers, MD

Working Group Assignment/Chair: Acute/Pooja Khatri, MD

Date Protocol Synopsis received to Dr. Kleindorfer: 5/22/14

Date query submitted to website: 5/28/14

Any queries to Investigator to clarify criterion? If so, dates of contact: Yes, emails on 5/22, 5/28

Date of Final Report delivered to Working Group Chair: 6/4/14

Description of the Greater Cincinnati Population:

The Greater Cincinnati/Northern Kentucky (GCNK) region includes two southern Ohio counties and three contiguous Northern Kentucky counties that border the Ohio River, which contains a bi-racial population of 1.3 million. Only residents of the five study counties are considered for case ascertainment. In the GCNK region, 19 hospitals were active in 1993/94, 18 in 1999, and 17 in 2005. Previous studies have documented that residents of the five counties who have a stroke exclusively seek care at these hospitals rather than at hospitals in the outlying region. Our study population is largely representative of the United States with regard to median age, percent of blacks, median household income, and percent of population below the poverty level. Every hospitalized stroke (including IS, ICH, SAH, and TIA) are ascertained via a combination of hot-pursuit/symptom-based screening and ICD-9 discharge codes. A sampling of outpatient sites is also performed, including all coroner's offices. Charts are then abstracted by a study nurse, and final case determination and subtyping performed by a study physician.

Study period used: 2005

Subtype of stroke: Ischemic

ED-arriving or all: ED-arriving only

Exclusion Criterion	**Number ineligible**	**Number excluded with ONLY this criteria**
Age < 18 or > 80	518	10
NIHSS <8 or >=25	1458	225
Time > 11 hours	1037	37
mRS >=2	925	56
Pacemaker	107	3
AICD	16	0
Creatinine >2.0	140	0
INR>1.5	108	2
Platelets <100K	29	1
PTT>50	47	2
Denominator	1843	
Excluded	1797	
Eligible (%)	46 (2.4%)	

If applicable, % eligible of otherwise tpa-eligible ischemic strokes: n/a

Assumptions based on protocol synopsis and discussions with investigators:

- NIHSS is based on retrospective chart review, based on validated methods (Williams, et al).
- Ability to have an MRI was limited to only excluding those patients with pacemakers or AICD. Other metal/MRI contraindications were not available.
- Time from symptom onset was set as >11 hours, based on the described time window of 12 hours, allowing 1 hour for an MRI to be obtained and angiographic access. This was agreed upon by the investigator.
- PTT > 50 was added by Dr. Kleindorfer as another indicator of anticoagulation, this could be removed if requested.

Criteria not included in this assessment (those of possible importance bolded by Dr. Kleindorfer):

- **MRI demonstrates Target Mismatch Profile and large vessel occlusion**: we estimate that this has the potential to exclude large numbers of patients in this potential cohort. PI is sending literature to estimate this.
- Other hematologic dyscrasias, or vasospastic disorders, (we did not search text fields)
- Known allergy to iodine previously refractory to pretreatment medications
- Other serious, advanced, or terminal illness
- Pre-existing medical, neurological or psychiatric disease that would confound the neurological or functional evaluations.

Variations in exclusion criteria and their impact on eligibility:

The three most common exclusions were: stroke severity, time from symptom onset, and baseline disability (with age being the next most common).

Describe how changing key criteria might impact eligibility: we did a detailed analysis of this and found the following eligibility rates (baseline 2.4% as originally submitted):

Decrease NIHSSS to 6 only: 3.5%

Increase age to 85 only: 2.9%

Allow mRS of 0,1,2 only: 4.1%

Doing all three of the above: **6.3%**

Therefore, we found that by making all three of the changes above, the medical eligibility is relatively increased by 150%.

Note: These eligibility calculations do not take into account ability to consent, availability of services/off-hour enrollments at centers, experience and enthusiasm of the investigators, and competing trials.

Summary of Eligibility Analysis Within a Population: As initially submitted, there were extremely few patients eligible for this trial within a population, at approximately 2.4% of ED-arriving ischemic strokes. Especially concerning is the requirement for MRI mismatch, which we have not included in this assessment, but will likely significantly further limit the eligible patients available. Specific suggestions to improve the eligibility include lowering the NIHSS cut-off, increasing the upper age limit, and allowing slightly more disabled patients to be included.

Analysis performed by: Charles Moomaw, PhD

Report Prepared by: Dawn Kleindorfer, MD