Data Supplement 1

Hospital and Emergency Department Characteristics detail

Neurology consultation rates were not uniform across the hospitals. Hospital 1's protocol specified notification of the neurology resident (considered a neurology consultation for the purposes of the study) as part of their training purposes and as they were the primary admitting service for tPA-treated patients. At the other three hospitals, patients were admitted under non-neurology attending physicians, with neurology acting as a consultant service only when requested.

Only very limited data are available on the radiology personnel performing the initial pre-treatment CT interpretation and the process used. This is due in part to the lack of available documentation on preliminary interpretations ("wet reads") often used in time-critical conditions and technological developments over the duration of the study which dramatically changed the process of after-hour CT interpretation (e.g. the use of remote teleradiology systems). CTs are known to have been interpreted by attending radiologists, radiology residents, and teleradiology staff. The availability or use of specialized neuroradiologists over the course of the study is unknown.

Case selection detail

All cases identified in a participating emergency department as treated with intravenous tPA for presumed ischemic stroke were included in the data collection. This included patients initially evaluated or treated in the ED at a non-participating hospital and subsequently transferred to a study hospital emergency department. Four methods of case ascertainment were used.

First, hospital billing code data were reviewed to identify thrombolytic use in stroke. Patients with any ICD-9-CM diagnosis code for cerebrovascular disease (430 – 437; 997.02) and

a procedure code for thrombolytic use (99.10 or CPT codes 37195 or 37201) were identified. The use of codes including cerebral hemorrhage was intentional to identify patients potentially coded for a hemorrhagic complication of stroke treatment instead of their initial stroke. A search for Diagnostic Related Groups 14 and 15 (cerebrovascular disease) and a code for thrombolytic use (99.10) was conducted as well.

Second, all hospital pharmacy logs identifying tPA use in the emergency department were reviewed. This included both paper and computerized (Omnicell, Pyxis) pharmacy dispensing logs and/or pharmacy charge reports.

Third, all site-specific stroke registries/logs maintained for quality assurance/quality improvement purposes were reviewed. These were available for all four sites as part of their internal quality assurance processes.

Fourth, the Paul Coverdell National Acute Stroke Registry data was reviewed. This Centers for Disease Control supported registry used an active surveillance method during a portion (May-November 2002) of the case ascertainment period to screen for thrombolytic use in stroke and contained data on tPA use at hospitals 1 and 2 (Table 1).

Data quality detail

Twenty percent of charts from each site were systematically selected for dual data abstraction by independent reviewers to assess inter-rater agreement. The method of adjudication of disagreements between charts was determined by the data field involved in the disagreement.

Each data field was designated *a priori* as either “critical” or “non-critical”. Critical data fields represented outcome or safety measures (e.g. presence of ICH on neuroimaging, tPA inclusion/exclusion characteristics, discharge status), while non-critical fields represented elements such as past medical history, EMS times, etc.

Disagreements on “critical” data elements were adjudicated by consensus of two physician investigators following review of original source material. For “non-critical” data elements, a single physician investigator, experienced in acute stroke care, adjudicated disagreements. By study protocol, inter-rater of agreement of less than 90% for critical data elements in the 20% initially sampled would have mandated dual data abstraction of all records.

Table. Revised Safety and Efficacy Outcomes.[§]

	Unadjusted				Adjusted*			
	Community v. NINDS treatment		**Community v. NINDS placebo**		**Community v. NINDS treatment**		**Community v. NINDS placebo**	
One-year mortality (Cox model) HR (95% CI)	1.20	(0.87-1.66)	0.97	(0.71-1.33)	1.26	(0.90-1.78)	0.91	(0.65-1.28)
Intracerebral Hemorrhage (sICH within 36 hrs) OR (95% CI)	1.12	(0.58-2.17)			1.12	(0.55-2.28)		
Functional recovery (mRS ≤ 2) OR (95% CI)	0.83	(0.53-1.31)	1.46	(0.98–2.18)	0.66	(0.38-1.17)	1.03	(0.64-1.67)

[§]Safety and efficacy outcomes after eliminating 22 patients who received t-PA prior to transfer to one of the four study hospitals.

*Outcomes adjusted for baseline variables: age, diabetes, stroke severity and prior stroke.

sICH = significant/symptomatic intracerebral hemorrhage, HR = Hazard Ratio; OR = Odds Ratio