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A Prehospital Acute Stroke Trial Has Only Modest Impact on Enrollment in Concurrent, Post-Arrival-Recruiting Stroke Trials

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Abstract

Background: Because “time is brain,” acute stroke trials are migrating to the prehospital setting. The impact upon enrollment in post-arrival trials of earlier recruitment in a prehospital trial requires delineation.

Methods: We analyzed all patients recruited into acute and prevention stroke trials during an 8-year period when an academic medical center (AMC) was participating in a prehospital treatment trial – the NIH Field Administration of Stroke Treatment – Magnesium (FAST-MAG) study.

Results: During the study period, in addition to FAST-MAG, the AMC participated in 33 post-arrival stroke trials: 27 for acute cerebral ischemia, one for intracerebral hemorrhage, and 5 secondary prevention trials. Throughout the study period, the AMC was recruiting for at least 3 concurrent post-arrival acute trials. Among 199 patients enrolled in acute stroke trials, 98 (49%) were in FAST-MAG and 101 (51%) in concurrent, post-arrival acute trials. Among FAST-MAG patients, 67% were not eligible for any concurrent acute, post-arrival trial. Of 134 patients eligible for post-arrival acute trials, 101 (76%) were enrolled in post-arrival trials and 32 (24%) in FAST-MAG. Leading reasons FAST-MAG patients were ineligible for post-arrival acute trials were: NIHSS too low (23.4%), intracranial hemorrhage (17.9%), IV tPA used in standard management (9.0%), NIHSS too high (7.1%), and age too high (5.2%).

Conclusions: A prehospital hyperacute stroke trial with wide entry criteria reduced only modestly, by one-fourth, enrollment into concurrently active, post-arrival stroke trials. Simultaneous performance of prehospital and post-arrival acute and secondary prevention stroke trials in research networks is feasible.

Keywords

Acute stroke trials; Trial design; Prehospital trials; FAST-MAG; Clinical trials; Concurrent trials

Introduction

Because “time is brain,” acute stroke trials are increasingly migrating to the prehospital setting.^{1–5} While some research interventions, such as neuroprotective agents, are well-suited for paramedic, prehospital delivery without brain imaging, other interventions, including fibrinolytics, endovascular therapies, and surgical procedures, can only be tested after brain imaging or after hospital arrival. Regulatory agencies generally prefer that clinical studies avoid enrolling patients concurrently in two different therapeutic trials, to avoid uncertainty in ascription of benefit and harm to each research therapy.^{6, 7} Restricting enrollment to only one trial at a time raises the concern that prehospital recruitment of patients into ambulance-based trials may lead to a major reduction of patients available for enrollment into Emergency Department (ED)- and hospital-based trials.

However, there are several reasons that prehospital trials may have only a modest impact upon recruitment into post-arrival-recruiting trials. Substantial proportions of acute stroke patients are not available for prehospital recruitment for various reasons, including: 1) they arrive by private vehicle, rather than 911 ambulance; 2) aphasia or confusion render them unable to provide medical history, and a knowledgeable informant is not available to provide this information until after ED arrival; 3) aphasia or confusion render them unable to provide explicit research informed consent, and a legally authorized representative is not available to provide proxy consent until after ED arrival; 4) the entry criteria for the prehospital trial(s) and post-arrival trial(s) differ and some patients are only eligible for post-arrival trials; and 5) the entry criteria for the prehospital trial(s) and post-arrival trial(s) are overlapping, but some patients are too mildly or severely affected to qualify for trial entry in the prehospital setting, but then worsen or improve into eligibility range post-arrival.

The goal of this study is to quantify the impact of prehospital stroke trial recruitment on enrollment in concurrently active, post-arrival trials of diverse interventions for cerebrovascular conditions.

Methods

We analyzed all inpatients enrolled in acute and secondary prevention stroke trials at an academic medical center (AMC) during the time period in which the AMC was participating in a prehospital treatment trial, as well as multiple concurrent post-arrival trials. We quantified the number of inpatients enrolled in the prehospital trial and the post-arrival trials. In addition, for each subject enrolled in the prehospital study, we evaluated whether they would have met criteria for entry into any concurrently-recruiting post-arrival trials, had they not been enrolled in the ambulance-based trial.

The post-arrival trials analyzed were studies of acute therapies, and secondary prevention therapies, for ischemic stroke (IS), transient ischemic attack (TIA), or intracerebral hemorrhage (ICH). Post-arrival trials enrolling subarachnoid hemorrhage patients were not analyzed because the FAST-MAG enrollment criteria were designed to capture acute neurovascular conditions that most commonly present with focal, rather than nonfocal, deficits.

Patient eligibility for all trials active at the time of their presentation was determined based on patient characteristics abstracted from the medical record and study case report forms, and the specific inclusion and exclusion criteria of each trial. Patient information analyzed included age, NIH Stroke Scale (NIHSS) score on ED arrival, stroke subtype, time from last known well to ED arrival, and whether or not the patient received tPA or endovascular treatment as part of conventional medical care.

The prehospital trial active during the study period was the Field Administration of Stroke Therapy–Magnesium (FAST-MAG) phase 3 trial, a multicenter, randomized, double-blind, placebo-controlled, clinical trial enrolling patients 40 to 95 years of age with suspected stroke as determined with the use of the modified Los Angeles Prehospital Stroke Screen (LAPSS). Patients had to be within 2 hours of last known well time, and have unilateral motor deficits, which could be due to either acute cerebral ischemia or acute intracranial hemorrhage. Detailed descriptions of FAST-MAG entry criteria, enrollment processes, and results have been previously published.^{2, 8, 9} All trials, including FAST-MAG, recruited patients 24 hours a day, 7 days a week. Throughout the study period, all patients identified as eligible for FAST-MAG were offered enrollment in FAST-MAG, regardless of whether they might turn out to be also be eligible for concurrently available in-hospital trials. Precedence was given to FAST-MAG to ensure smooth, rapid enrollment in the field, and because full eligibility evaluation for other trials could not be completed in the prehospital setting.

In statistical analyses, normally distributed variables were characterized with mean and standard deviations and non-normal variables with medians and interquartile range. The impact of prehospital trial recruitment upon recruitment for in-hospital trials was quantified using point values and 95% confidence intervals. In addition, impact upon recruitment was broadly characterized as: reduction by 1–25% - modest; reduction by 26–50% - moderate; reduction by 51–100% - severe. These definitions are based on range definitions in prior studies assessing discordance between planned and actual recruitment, and studies assessing site-level variations in recruitment rates.^{10–12}

Results

The academic medical center site participated in the prehospital FAST-MAG study throughout the trial-wide enrollment period, from January 2005 – December 2012. During this 96-month interval, the AMC also participated in 33 post-arrival stroke trials, including 27 of acute ischemic stroke interventions, 1 of an acute intracerebral hemorrhage intervention, and 5 of secondary prevention.

For the 28 post-arrival acute trials (Figure 1), the length of time during which each was actively enrolling concurrent with prehospital FAST-MAG trial recruitment was a median of 19 months (IQR 9–43). During the period in which the prehospital FAST-MAG trial was actively enrolling, a mean of 6.5 (SD $\pm$ 3.2, range 3–9; IQR 6–8) post-arrival recruiting trials were actively enrolling at the same time.

Features of the 28 acute treatment, post-arrival recruiting stroke trials are shown in Table 1. Of the 27 acute cerebral ischemia trials, the experimental interventions were endovascular reperfusion in 9 (33%), intravenous fibrinolytic in 9 (33%), neuroprotective in 7 (26%), antithrombotic in 4 (15%), and other in 1 (4%). The intracerebral hemorrhage trial tested a hemostatic drug. Among the acute cerebral ischemia trials, the upper limit of the time window after last known well in which patients could be recruited ranged from 3 to 48 hours (median 8, IQR 6–12). For the acute ICH trial the upper limit was 3 hours from last known well time (LKWT).

During the period of prehospital FAST-MAG trial enrolling, 199 patients were enrolled in acute stroke trials at the AMC, including 98 (49%) in FAST-MAG trial and 101 (51%) in concurrent, post-arrival acute trials. Of the 98 patients enrolled in FAST-MAG, 66 (67.3%) were not eligible for any post-arrival trial that was active at the time of their enrollment in the prehospital trial. Reasons for ineligibility for concurrently active post-arrival are presented in Table 2. Most common were: NIHSS too low (23.4%), intracranial hemorrhage (17.9%), deficit resolved to TIA (9.2%), IV tPA used in standard management (9.0%), NIHSS too high (7.1%), and age too advanced (5.2%).

Of the 32 patients enrolled in FAST-MAG who would otherwise have been eligible for a concurrent, post-arrival acute trial, 15 (15.3%) were eligible for one post-arrival trial, 7 (7.1%) for 2 trials, 6 (6.1%) for 3 trials, and 4 (4.1%) for 4 trials. Accordingly, the FAST-MAG trial reduced enrollment in concurrent post-arrival acute trials by at most 24.1% [32/(32+101)]. Among the 28 post-arrival acute stroke trials, enrollment windows were: 0–3h for 5 trials, 0–6/9h for 11 trials, 3–9h for 4 trials, 0–12/24 for 6 trials, 8–24h for 1 trial, and 0–48h for 1 trial. Within different time frames, enrollments in the FAST-MAG trial reduced enrollments in concurrent post-acute trials by: 0–3h trials – 61% (22/36); 0–6h trials – 0% (0/6); 0–9h trials – 32% (18/57); and 0/8 – 24/48h trials – 14% (6/42).

During the FAST-MAG study period, there also were 5 concurrent secondary prevention trials. All trials focused on cerebral ischemia patients rather than intracerebral hemorrhage patients, and differed in the breadth of stroke mechanisms targeted. The trials tested: patent foramen ovale closure devices for otherwise cryptogenic cerebral ischemia (2 trials), stenting versus endarterectomy for symptomatic cervical carotid disease (1 trial), stenting versus aggressive medical therapy for symptomatic intracranial atherosclerotic disease (1 trial), and different antiplatelet regimens for non-cardioembolic cerebral ischemia (1 trial).

For these 5 secondary prevention trials, the length of time during which each was actively enrolling concurrent with prehospital FAST-MAG trial recruitment was median 42 months (IQR 39–53). During the 8-year period in which the prehospital FAST-MAG trial was actively enrolling, one or more secondary prevention trials were actively enrolling during 100% of the time period (including 2 or more during 86.3% of the time period). Among these 5 trials, 4 permitted enrollment more than 90 days after qualifying stroke, potentially allowing patients to be sequentially enrolled in the prevention trial after completing their 3 month final FAST-MAG study visit. One trial (Stenting versus Aggressive Medical Therapy for Intracranial Arterial Stenosis - SAMPPRIS) permitted enrollment only up until 30 days after the qualifying event.

Among the 98 patients enrolled in FAST-MAG, 1 (1%) was subsequently enrolled in a secondary prevention trial after completing the 90-day exit visit for FAST-MAG. Of the 97 patients not enrolled in a concurrent secondary trial, 91 (93.8%) did not meet eligibility for an active secondary prevention trial, regardless of participation in FAST-MAG. Among these 91 patients, leading reasons for ineligibility were: trial eligibility confined to acute cerebral ischemia and event was ICH or mimic (21.2%); mechanism of cerebral ischemia did not match study entry criteria (65.6%); out of age range (1.7%); patient expired during acute hospitalization (3.3%); and “other” (8.3%).

Discussion

This study demonstrates that a prehospital stroke trial with wide entry criteria reduced only modestly, by about one-fourth, enrollments into concurrently active, post-arrival acute stroke trials. Most patients enrolled in FAST-MAG were ineligible for any simultaneously running post-arrival acute stroke trial, with the most common reasons for lack of eligibility being mild stroke deficits, intracranial hemorrhage stroke subtype, and use of tissue plasminogen activator as clinically indicated therapy. In addition, the prehospital stroke trial had virtually no impact on enrollment in concurrently active secondary prevention stroke trials, excluding only about 6% of prehospital trial-enrolled patients from secondary prevention trial eligibility.

These findings complement and extend a prior investigation of determinants of enrollment in acute stroke trials. In a meta-analysis of 32 acute ischemic stroke trials, the leading determinants of higher rates of enrollment were inclusion of patients with mild stroke deficits and of patients with longer times from onset to enrollment.¹³ The influence of concurrently active trials was not investigated. The higher recruitment rates for trials with enrollment windows more than 6 hours after last known well accords with the findings in the current study that substantial volume of patients could be enrolled in other acute trials even while FAST-MAG was recruiting, as the prehospital trial had a very short permitted window of 2 hours from onset to enrollment. It is likely that the preponderance of prehospital acute stroke trials in the future will similarly have very brief enrollment windows, as the additional burden of conducting a trial in the prehospital setting is only worth undertaking when the treatment being tested is aimed for the hyperacute first 1–3 hours after onset.

In this study, there was a differential impact of the prehospital trial upon recruitment for post-arrival acute stroke trials according to the permitted enrollment time windows of the post-arrival trials. The recruitment reductions were substantial for post-arrival trials focused upon the first 3 hours after onset, mild to moderate for post-arrival trials focused upon the first 6–9 hours after onset, and mild for post-arrival trials focused upon the first 24–48h after onset. While all post-arrival trials could enroll patients who were ineligible for FAST-MAG, because they arrived by private vehicle, could not be fully assessed in the ambulance, or had specific, non-time-related FAST-MAG study exclusion criteria, trials with later permitted enrollment time windows could also enroll patients who presented to the EMS system too late for FAST-MAG entry, but were otherwise FAST-MAG eligible.

This study confirms that participation in multiple trials concurrently is a common practice at academic stroke centers. Participation in several trials simultaneously allows centers to use a single screening process to efficiently identify patients for studies with non- or minimally-overlapping entry criteria, handle the frequent unexpected holds or terminations that occur for any single trial, and address the relative paucity of centers with sufficient expertise and commitment to participate in any acute study. The National Institute of Health has funded national networks of centers for stroke trials with the requirement that centers be able to participate in multiple trials concurrently in order to meet this substantial need. Several studies have addressed how centers may handle enrollment of patients who are eligible for more than one trial simultaneously, and identified as a key aspect that patients be assigned to one or another trial based on neutral features, such as randomized selection of study to be offered, alternating offering of one study and then the next, and assigning specific days or weeks for each study to be offered.^{14–16} Assignment to one or another concurrently available trial, in contrast, should not be based on investigator hypothesis as to which of the experimental intervention would work best for that particular patient, as that could skew the representativeness of the populations enrolling in each trial and confound interpretation of trial results. The case of prehospital trials co-existing with post-arrival trials is only partially addressed by this prior work. At the time of enrollment in the field, the patient is eligible for only one trial – the trial that permits enrollment in the field. Accordingly, following the rule that patients eligible for only a single trial should be enrolled in that trial, the prehospital patient should be offered enrollment in the field study.

Nonetheless, the concern naturally arises that a concurrent prehospital trial may deplete in-hospital trials of patients in general, and of very early post-onset patients in particular. A theoretical approach to handle this overlap would be to identify those patients in the field who meet entry criteria for a post-arrival trial, and neutrally selecting some of these patients to not be offered enrollment in the field study, so they may be offered enrollment in the post-arrival trial. However, there are several practical drawbacks to such a selective field enrollment strategy. First, eligibility for the in-hospital trial would be the conditional upon the patient not substantially improving or deteriorating between the time of prehospital versus post-arrival evaluation. However, one-third of stroke patients do improve or deteriorate between the time of paramedic and in-hospital evaluation, so a particular patient cannot be securely assessed in the field as destined to also be eligible for an in-hospital trial after arrival.¹⁷ Second, in-hospital trials often have very detailed entry criteria that require more time and/or testing to assess than is available in the prehospital setting, again making judgment of eligibility of a field patient for an in-hospital trial uncertain. In contrast, prehospital trials are designed using simple entry criteria that can be rapidly and reliably applied in the ambulance setting.

Fortunately, the current study shows prehospital trials will produce only a modest overall decrement in the number of patients who can be enrolled in concurrently, active, post-arrival-enrolling clinical trials. The impact of the prehospital trial is mitigated by several factors. First, some acute stroke patients arrive at the study hospital by private transport or by interfacility transfer, rather than by direct EMS transport from the field. These patients are not encountered by the 911 EMS system and so will not be enrolled in a prehospital study. Second, for prehospital studies using explicit informed consent, some patients, whose

strokes have rendered them not competent to provide consent, may not have a legally authorized representative available on scene who can provide consent for enrollment, but may have their legally authorized representative later arrive to the Emergency Department and able to provide research consent for an in-hospital trial. Even for prehospital trials using exception from informed consent, some patients, whose strokes have rendered them unable to provide a detailed medical history adequate to determine if they meet entry criteria for the prehospital study, may not have an individual who knows them well available on scene who can provide historical information, but may have a reliable informant later arrive to the Emergency Department and able to provide fuller history permitting enrollment in an in-hospital trial. Third, some patients' neurologic deficits will worsen or improve between the time of first paramedic encounter and ED arrival, potentially migrating them from study ineligibility to eligibility only upon arrival. Fourth, due to differing entry criteria, a patient may only be eligible for the in-hospital and not prehospital trial.

Additionally, co-enrollment of patients in concurrent clinical trials is appropriate for certain types of interventions. Sequential enrollment is a straightforward option, with enrollment in a second trial occurring once a patient has entirely completed participation in the first trial. For example, patients may be enrolled in the prehospital trial and then, after they exit after the 3 month outcome, proceed to being enrolled a long-term secondary prevention trial. Sequential enrollment occurred in one patient in the current cohort. Simultaneous participation in more than one trial poses more challenges, but is also possible in select circumstances. While regulatory concerns must be carefully addressed regarding correct attribution of beneficial and harmful effects to each particular intervention under study, scientific, ethical, and regulatory frameworks have been developed that enable co-enrollment in concurrent trials to proceed with interpretive validity.^{18,19}

This study has limitations. The analysis was focused on one stroke receiving center; generalizability of findings to other localities needs to be confirmed in future studies. The enrollment criteria in FAST-MAG were extremely broad for a stroke trial, including a wide range of deficit severity and patient age.²⁰ Prehospital trials with stricter entry criteria would have even less impact on recruitment into concurrent in-hospital trials than seen in the present report.

In conclusion, a prehospital hyperacute stroke trial with wide entry criteria reduced only modestly, by one-quarter, overall recruitment into concurrently active, post-arrival stroke trials, though the impact upon post-arrival, under 3 hour-recruiting trials was substantial. These findings indicate that simultaneous performance of prehospital and post-arrival acute and secondary prevention stroke trials in research networks is practicable.

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Figure 1.

Concurrent, post-arrival acute stroke trials during the FAST-MAG enrollment period

Table 1:

Concurrent post-arrival acute trials during the FAST-MAG enrollment period, 01/2005–2012

Study Name	Stroke Type	Time Window (from onset)	Treatment Type	Enrollment Start	Enrollment End	Patients Enrolled (n)	Patients Not Enrolled Due to FAST-MAG (n)
ONO	AIS	< 6 hrs	Neuroprotective	12/30/2003	5/11/2005	0	0
AbESTT II	AIS	< 5 hrs 30 min	Antithrombotic	5/21/2004	9/17/2005	1	0
IMS II	AIS	< 3 hrs	Fibrinolytic, Endovascular Mechanical	1/1/2003	4/26/2006	1	0
SAINT II	AIS	< 6 hrs	Neuroprotective	1/3/2005	6/15/2006	0	1
Multi MERCI	AIS	< 8 hrs	Endovascular Mechanical	12/20/2004	7/26/2006	11	1
SUN	AIS	< 6 hrs OR < 9 hrs	Neuroprotective	9/11/2006	10/24/2006	0	0
FAST	ICH	< 3 hrs	Other (Prothrombotic)	1/19/2006	11/3/2006	1	0
DIAS 2	AIS	3–9 hrs	Fibrinolytic	7/26/2005	12/8/2006	5	0
TS011-US104	AIS	<24 hrs	Neuroprotective	9/26/2005	5/12/2007	7	0
CLEAR	AIS	< 3 hrs	Fibrinolytic, Antithrombotic	8/15/2003	5/23/2007	1	0
ALIAS	AIS	< 5 hrs	Neuroprotective	9/26/2006	12/4/2007	3	0
NUVELO	AIS	3 – 9 hrs	Fibrinolytic	10/22/2007	3/17/2008	0	0
NEST-2	AIS	< 24 hrs	Endovascular Mechanical	10/15/2007	4/14/2008	1	0
VASTT	AIS	3 – 9 hrs	Fibrinolytic	4/6/2008	8/27/2008	1	0
Flo24	AIS	8 – 24 hrs	Endovascular Mechanical	5/11/2007	9/15/2008	6	0
ANCROD	AIS	< 6 hrs	Fibrinolytic	5/22/2006	12/16/2008	3	0
SENTIS	AIS	< 14 hrs	Endovascular Mechanical	6/15/2006	1/31/2010	14	0
SWIFT	AIS	< 8 hrs	Endovascular Mechanical	7/15/2010	2/18/2011	4	3
Mitsubishi	AIS	< 8 hrs	Neuroprotective	7/2/2008	3/10/2011	0	4
TREVO 2	AIS	< 8 hrs	Endovascular Mechanical	8/22/2011	12/2/2011	1	0
MR RESCUE	AIS	< 8 hrs	Endovascular Mechanical	6/17/2004	12/5/2011	16	13
IMS III	AIS	< 3 hrs	Fibrinolytic	1/3/2007	4/18/2012	9	12
CLEAR-ER	AIS	< 3 hrs	Fibrinolytic, Antithrombotic	10/19/2009	10/5/2012	2	21
PAO	AIS	< 18 hrs	Endovascular Mechanical	4/20/2008	12/18/2012	0	0
GMAIS	AIS	< 18 hrs	Neuroprotective	10/3/2011	5/24/2013	3	4

Study Name	Stroke Type	Time Window (from onset)	Treatment Type	Enrollment Start	Enrollment End	Patients Enrolled (n)	Patients Not Enrolled Due to FAST MAG (n)
CUFFS	AIS	< 48 hrs	Other (External Counterpulsation)	3/22/2010	6/13/2013	1	2
DIAS 4	AIS	3 – 9 hrs	Fibrinolytic	7/26/2010	7/7/2014	0	0
POINT	AIS/TIA	< 12 hrs	Antithrombotic	2/16/2011	Current	10	1
Total						101	N/A

ONO - Randomized, Double-Blind, Placebo-Controlled Trial, Multi-Center Effects of ONO-2506 Intravenous Infusion on the Amelioration of Neurological Damage and Improvement of Stroke Assessment Scale Scores in Patients with Acute Ischemic Stroke

AbESTT II - Abciximab (ReoPro®) in Acute Ischemic Stroke: A Phase III, Multinational, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial

IMS II - Interventional Management of Stroke II

SAINT II - A Double Blind, Randomized, Placebo Controlled, Parallel Group, Multicenter, Phase IIb/III Study to Assess The Efficacy and Safety of Intravenous NXY-059 in Acute Ischemic Stroke

Multi MERCI - A Multinational-Controlled Registry to Evaluate the Concentric MERCI Retriever System

SUN- A Phase IIb Randomized, Double-Blind, Placebo-Controlled, Group-Sequential, Multicenter Dose Finding Study of the Safety and Efficacy of SUN N4057 (Piclozotan) Administered for 72 Hours by Continuous Intravenous Infusion in Subjects with Acute Ischemic Stroke and Measurable Penumbra on MRI

FAST - A Randomized, Double-blind, Placebo-controlled, Multi-Center, Parallel- Groups Confirmatory Efficacy and Safety Trial of Activated Recombinant Factor VII (Novoseven/Niastase) in Acute Intracerebral Hemorrhage

DIAS II - A Prospective, Randomized, Double-Blind, Placebo-Controlled, Single Bolus, Multinational, Multi-Center, Parallel-Group Dose Ranging Study of Desmoteplase (INN) in the Indication of Acute Stroke

TS011-US104 - A Multicenter, Randomized, Double- Blind, Placebo- Controlled, Ascending- Dose Study of the Safety, Pharmacokinetics, and Pharmacodynamics of a Single, One- Hour Infusion of TS-011 in Acute Ischemic Stroke (AIS) Patients

CLEAR - Combined Approach to Lysis utilizing Eptifibatide and rt-PA in Acute Ischemic Stroke

ALIAS - A Phase III, Randomized, Multicenter, Clinical Trial of High-Dose Human Albumin Therapy for Neuroprotection in Acute Ischemic Stroke

NUVELO - A Phase II, Multicenter, Open-Label, Two Stage Study to Evaluate the Safety and Efficacy of Intra-Arterial Catheter-Directed Altimeprase for Restoration of Neurologic Function and Rapid Opening of Arteries in Stroke (CARNEROS-1)

NEST-2 - Neurothera Effectiveness and Safety Trial-2 (NEST-2), a Double-Blind, Randomized, Controlled, Parallel Group, Multicenter, Pivotal Study to Assess the Safety and Effectiveness of the Treatment of Acute Ischemic Stroke with the Neurothera® Laser System within 24 Hours from Stroke Onset

VASTT - Stenting versus medical treatment in patients with symptomatic vertebral artery stenosis: a randomised open-label phase 2 trial

Flo24 - Safety and Efficacy of NeuroFlo in 8–24 Hour Stroke Patients

ANCROD - A Randomized, Double-Blind, Placebo-Controlled Study of Viprinex™ (Ancrod Injection) in Subjects Beginning Treatment within 6 Hours of the Onset of Acute, Ischemic Stroke

SENTIS - Safety and Efficacy of NeuroFlo Technology in Ischemic Stroke

SWIFT - SOLITAIRE™ FR with the Intention for Thrombectomy (SWIFT) Study

Micro Therapeutics, Inc.

Mitsubishi - A Phase I. Double-Blind, Placebo-Controlled, Ascending Dose, Clinical Study Investigating the Safety, Tolerability, and Pharmacokinetics of MP-124 in Acute, Ischemic Stroke Patients

TREVO 2 - Thrombectomy Revascularization of Large Vessel Occlusions in Acute Ischemic Stroke

MR RESCUE - A Trial of Imaging Selection and Endovascular Treatment for Ischemic Stroke

IMS III - Interventional Management of Stroke III

CLEAR ER - Study of the Combination Therapy of Rt-PA and Eptifibatide to Treat Acute Ischemic Stroke

PAO - Feasibility and Safety of NeuroFlo in Patients with Persistent Arterial Occlusion (PAO) After Attempted Thrombectomy with Merci® Retriever System

GMAIS – A Phase 2, Double-Blinded, Randomized, Placebo Controlled Dose Escalation Study to Evaluate the Efficacy and the Safety of GM602 in Patients with Acute Middle Cerebral Artery Ischemic Stroke

CUFFS – Feasibility and Safety of Using External Counterpulsation (ECP) to Augment Cerebral Blood Flow in Acute Ischemic Stroke – the CUFFS Trial

DIAS 4 - A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Phase III Study to Evaluate the Efficacy and Safety of Desmoteplase in Patients with Acute Ischemic Stroke

POINT - Platelet-Oriented Inhibition in New TIA

Table 2:

Most common reasons FAST-MAG patients were ineligible for concurrent post-arrival acute trials

Reason	N (%)
NIHSS too low	122 (23.4)
Intracranial hemorrhage	93 (18)
Deficit resolved to TIA	48 (9.2)
Received IV-tPA as standard care	47 (9.0)
NIHSS too high	37 (7.1)
Age too high	27 (5.2)
Other	147 (28.2)

NIHSS: National Institutes of Health Stroke Scale

TIA: transient ischemic attack

IV-tPA: intravenous tissue plasminogen activator