In the past several months, we have crossed two important milestones—enrollment of 250 subjects, which is nearly the halfway point for the first interim analysis, and activation of our 50th site.

Since the beginning of the second year of the trial in August 2012, enrollment has consistently increased each quarter. By the first quarter of year 3, our average monthly enrollment reached 23 subjects per month. This is nearly where we need to be to meet our current expected monthly enrollment target.

August 2013 was our best month for recruitment to date with 29 total enrollments. Congratulations to all of our SHINE sites for their efforts with site start-up, screening and enrollment to make this trend in increasing recruitment possible. In October, Ohio State’s Wexner Medical Center set a record high of 6 enrollments in one month. Kudos to their study team. Special congratulations to the teams at Texas and their spokes, Austin Seto and Austin Brackenridge, as well as OSF St. Francis on their recent first enrollments. Additionally, our thanks to the following recently activated SHINE sites: Lincoln MC, Maimonides MC and University Hospital of Brooklyn (SUNY Downstate); Valley Baptist MC (UT Houston); University of Arizona MC (Arizona); and Summa Akron City (Ohio State).

In the coming months, we welcome your feedback as we work to make the retraining experience more valuable by individualizing and making new resources available. Also, because we have reached a substantial number of subjects that have completed follow up, we will begin to focus on retention and will be including these details in the next quarterly recruitment reports.

Thanks for all that you do to support the SHINE trial.

Karen C. Johnston, MD, MSc, SHINE Administrative PI
On behalf of the SHINE team

SHINE Enrollment by Site—Nov 2013

SHINE Recruitment—Apr 2012-Nov 2013
Introducing the NYP Columbia SHINE Team

A big THANK YOU to the team at Columbia University Medical Center for their continued efforts to support SHINE. NYP Columbia currently leads SHINE enrollment nationwide.

Dr. Stephan Mayer attributes their recruitment success to their dedicated team and having investigators physically present 24/7. He also says that there is a Gladwellian tipping point after several enrollments where things begin to fall into a routine for the study team and nurses.

Pictured here are several of the nurses that are integral to SHINE trial success as well as the core SHINE team which includes Stephan Mayer, MD, Cristina Falo, PhD, Angela Velazquez, Emma Meyers, Christine Lesch, PharmD, and many other co-investigators.

Tips for CRF Completion

- Calculating Treatment Days 1-3 and End of Treatment Time—Day 1 begins at the time of randomization (0-24) hours, Day 2 is 25-48 hours, and Day 3 is 49-72 hours. The treatment period begins at the time of randomization. The End of Treatment visit takes place on the date that the study infusion was stopped.
- Hypoglycemic Event CRF—This CRF is only required when the BG is less than 70mg/dl (one per episode <70).
- Neurological Worsening CRF—This CRF is only required when the SHINE study definition for Neurological Worsening is met (>4 point increase in NIHSS that persists for 24 hrs (+/-4hrs)).
- Hospital Arrival for In-Hospital Strokes—The date/time of hospital arrival entered on the Eligibility CRF should be the actual date/time of hospital arrival (not the time of symptom onset).
- Unblinding—Please remember not to include notes that could unblind in the General Comments section.

Karen Briggs, SHINE Data Manager

Q: What are the reasons that a patient who is being considered for SHINE would be excluded due to the inability to obtain a full NIHSS?
A: When it is not possible to obtain a full NIHSS within 30 minutes of the time of randomization, potential candidates must be excluded from SHINE. Categories on the NIHSS may be untestable due to joint fusion or amputation at the proximal joint, intubation, or other barriers to producing speech.

In the case of amputation or joint fusion at the shoulder or hip, motor arm, motor leg, and the limb ataxia assessments are untestable. Note that only amputations or joint fusions at the proximal joint are untestable.

If a patient is intubated or has other physical barriers to producing speech, it is likely not possible to assess dysarthria within 30 minutes of the time of randomization. Also note that it is possible score a comatose patient by using coma scoring instructions.

Q: Do you have any information about how to fill out the Antithrombotic Medications form?
A: While protocols vary by site, the information below briefly describes unfractionated and low molecular weight heparin and provides common dosing regimens for reference.

#12: Unfractionated heparin: full dose anticoagulation — Heparin continuous infusion with dose adjusted to therapeutic PTT.
#13: Unfractionated heparin: DVT prophylaxis — Fixed dose (usually 5,000 units) given subcutaneously twice or three times daily.
#16: LMWH: full dose anticoagulation — Weight based dosing of LMWH (ex. Enoxaparin 1mg/kg sq BID).
#17: LMWH: DVT prophylaxis — Fixed low dose of LMWH (ex. Enoxaparin 40mg daily or 30mg sq BID).

NOTE: tPA is captured on Form 21-IVtPA and IA Therapy and should not be noted on Form 16-Antithrombotic Medications.

Common Dosing Regimens for LMWH & Factor Xa Inhibitors

<table>
<thead>
<tr>
<th>Antithrombotic Medications</th>
<th>DVT prophylaxis</th>
<th>Full dose anti-coagulation (systemic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enoxaparin (Lovenox®)</td>
<td>40mg SQ daily or 30mg SQ q12</td>
<td>1mg/kg SQ q12 or 1.5mg/kg SQ daily</td>
</tr>
<tr>
<td>Dalteparin (Fragmin®)</td>
<td>2,500 or 5,000 units SQ daily</td>
<td>150-200 units/kg SQ daily (max 18,000 units)</td>
</tr>
<tr>
<td>Fondaparinux (Arixtra®)</td>
<td>2.5mg SQ daily</td>
<td>5-10mg SQ daily</td>
</tr>
</tbody>
</table>

SHINE Training Resources

We are building a library of updated SHINE resources. Please email Katrina van de Bruinhorst (Katrina.vandebruinhorst @utsouthwestern.edu) with any resources that you use at your site or with requests for materials that would be helpful with new team members or retraining.

—Katrina van de Bruinhorst, SHINE Recruitment Specialist
**Intervention Group Meals (PO Diet) - Steps for Nurses**

1. Assess consumption ~ 20 min after start of meal
   - All or nearly all
   - Partial
   - None or nearly none

2. Document consumption in EMR or source doc.

3. Click Cover Carbs
   - All/nearly all → 60
   - Partial → 30

4. Enter carbs eaten (gm)

5. Meal insulin dose will display. Enter initials. Click OK.

6. Confirm GlucoStabilizer is counting down

7. Give SQ meal insulin.

8. Chart in medical record.

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**Total Enrollment: 20**

**I-SPOT Activated Sites: 41**

The lab manual was recently updated and includes information clarifying the timing of the 48 hour blood draw: “At the 48 hour draw, blood should be collected at the time of the scheduled finger stick closest to 48 hours post randomization. If the time of the scheduled finger stick coincides with a meal, the meal should be held until after the scheduled finger stick and blood draw.”

Thank you to all sites that are diligently screening SHINE enrollments for inclusion into the I-SPOT sub-study. Please continue to make sure that every eligible I-SPOT patient is enrolled.

—Hannah Reimer, I-SPOT Project Manager

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**Who to contact**

- Protocol questions - Amy Fansler - (434) 982-6027 or afc7h@virginia.edu
- Regulatory & site readiness - Arthi Ramakrishnan - (734) 936-2454 or arthiram@umich.edu
- Laptop questions - Amy Fansler - (434) 982-6027 or afc7h@virginia.edu
- WebDCU support - Karen Briggs - (843) 792-3980 or briggsk@musc.edu
- Education and training - Joy Pinkerton - (734) 232-2138 or joyp@umich.edu

24 hour emergency contacts:
- SHINE Study Hotline – 800-915-7320 (Ext 1: Pt on call, Ext 2: Safety Monitor)
- WebDCU Emergency Randomization Hotline - 1-866-450-2016