ATACH-II
Antihypertensive Treatment of Cerebral Hemorrhage

Volume 1, Issue 12 | April 2015

Greetings from Dr. Qureshi, Principal Investigator for ATACH-II

Dear ATACH-II Colleagues:

We started 2015 with the great news of reaching our goal of enrolling approximately 40 subjects per month. In January 2015 we enrolled 42 subjects, the highest enrollment in a given month since the beginning of this trial. I thank each and every one of you for working hard and making this possible.

In January 2015, we enjoyed meeting many of the U.S. ATACH-II investigators and coordinators during the Investigators' Meeting in Orlando, Florida. We look forward to meeting many more of you during the upcoming conferences and sharing your concerns, insights, and collaborating toward resolutions.

The Data and Safety Monitoring Board (DSMB) for ATACH-II trial met by teleconference on February 23 2015, to review the safety and overall progress of the trial. The DSMB found everything to be satisfactory and recommended that the study proceed as planned. As of April 30, 2015 we have enrolled 883 of the required 1280 subjects. We are very encouraged by the increased enrollment in 2015 and remain cognizant of the timeline to complete enrollment. I continue to appreciate your hard work and commitment to the ATACH-II trial in achieving this goal.

I wish you all a very happy and enjoyable summer!

Warmest regards,

Adnan I. Qureshi, M.D.

Inside this Issue...

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ATACH-II Site Leaderboard as of April 30, 2015

Rank	Site Name	Country	No.	Principal Investigator(s)	Primary Study Coordinator
1	National Cerebral and Cardiovascular Center	Japan	72	Toyoda, Kazunori	Hirase, Kanae
2	Beijing Tiantan Hospital	China	69	Wang, Yongjun	Ding, Zeyu
3	Kobe City Medical Center General Hospital	Japan	45	Sakai, Nobuyuki	Okitsu, Miyuki
4	Toranomon Hospital	Japan	33	Hara, Takayuki	Matsukami, Mihoko
5	The First People's Hospital of Taizhou	China	31	Wang, Zhimin	Chen, Jie
6	National Taiwan University Hospital	Taiwan	28	Jeng, Jiann-Shing	Wang, Yu-Ting
7	Columbia University	USA	26	Agarwal, Sachin & Lee, Kiwon	Falo, Cristina
8	St. Cloud Hospital	USA	25	Suri, M. Fareed K	Freese, Melissa
9	Abington Memorial Hospital	USA	23	Shah, Qaisar	Jonczak, Karin
10	New Jersey Neuroscience Institute, JFK Medical Center	USA	18	Kirmani, Jawad	Porbeni, Charles
10	Kaohsiung Veterans General Hospital	Taiwan	18	Lo, Yuk-Keung & Lin, Ching-Huang	Hsu, Yi-Ting
	Total Enrolled = 883				

International Leaderboard as of April 30, 2015

Rank	Country	Enrollments	Sites Released to Enroll
1	United States	381	65
2	Japan	248	13
3	China	128	4
4	Taiwan	81	7
5	Germany	31	9
6	South Korea	14	2

2015 Investigators' Meeting Awards to Domestic Sites

Top enrolling site 2011-2013: Abington Memorial Hospital

First 3 subjects were enrolled in this site, and was the top enrolling site for the first 3 years

Top Enrolling site 2014: Columbia University

Overall highest enrollment in the study to date

Top Enrolling New Site: Ochsner Clinic Foundation

Highest enrolling new site released to enroll in year 2014

First Telemedicine Enrollment & Top Enrolling in Timeline since RTE:

St. Cloud Hospital Hospital

First subject enrolled through use of telemedicine & top performing site for enrollment per amount of time since released to enroll (RTE)

2014 Top Enrolling New NETT Site 2014: Memorial Hermann

Top enrollment for new NETT site in calendar year 2014. Noted also for timeliness of data, compliance to protocol, and for preparing the most spokes

2014 Top Enrolling New NETT Hub-Spoke Complex:

Emory University/Grady Memorial Hospital

Enrollment opened at both new hub and new spoke, noted for speed to enroll, speed to release first spoke, timeliness of data/DCR responses, additional spokes preparing

Key Enrollment Information for ATACH-II

24-Hour Toll Free Hotline: 1-855-870-7205 *or* 952-225-0779
Tell the operator: Your name, site name, call back number

To randomize: https://dcu.musc.edu/atach2/

Friendly Reminders: By Kathryn France, PHN, CCRC, CCRA

About nicardipine use in ATACH-II:

A new study drug supply policy was recently posted in ATACH-II WebDCU™ in response to feedback from pharmacists at two newer US sites. At US sites, this form is filled out during the important, early conversation with the site pharmacist when implementing ATACH-II, and is also used to update information when re-ordering nicardipine. The form requires a signature from the site pharmacist, and now also clarifies that site study team members are responsible for overall staff training about nicardipine use at each enrolling hospital. This is true at all sites and is always an ongoing process, since staff members who may care for ATACH-II subjects are not always consistent due to staff rotations and personnel changes over time.

A variety of nicardipine products are available to meet needs across different ATACH-II sites around the world. By necessity, the nicardipine that will be used has to be in accord with drug regulatory approvals and the availability of various *nicardipine hydrochloride* products within each country. At US sites, *CARDENE® IV* is shipped directly from *Chiesi USA* as pre-mixed, ready-to-use ("RTU") bags and is provided free of charge, a potentially time-saving option helpful to the goals of this study. Even within the US, though, the safest product to use at any given site may vary according to what is listed in the hospital formulary, and what may therefore be programmed in to IV pump libraries. As a publicly-funded study, cost is always a consideration. Fortunately, a variety of generic vial products are available worldwide at relatively low cost, and the specific product chosen may therefore differ across sites, as may the capacity of site pharmacies to mix nicardipine IV drip solutions quickly enough for rapid use in ATACH-II enrollments. Because these factors change occasionally, it is important that the site pharmacist always be involved in the decision-making and ordering process for study-related nicardipine. These factors are also related to why a specified nicardipine product or concentration choice is not mandated by the study protocol.

For the most part, the use of nicardipine will be familiar to ED and ICU staff. Because SBP is lowered quite quickly and significantly in ATACH-II, the greater potential for hypotensive effects such as low urine output, tachycardia, and neurological deterioration, and also the subject's overall fluid balance require careful monitoring. Communicating safety considerations as well as requirements and goals of the protocol are important so that attending staff physicians and bedside nurses have increased awareness of these concerns in relation to the research being conducted. The importance and success of this education is evident when SBP graphs and adverse events are reviewed centrally in data collected for the trial at each site.

Unless a medical contraindication arises after enrollment, agents listing *nicardipine hydrochloride* as the single active ingredient should remain the primary medication used to control SBP in all ATACH-II subjects throughout the 24-hour study period. There are allowances for other IV antihypertensives to be used before enrollment, and for secondary (or occasionally tertiary) agent use when nicardipine does not adequately control SBP alone at its maximum 15 mg/hr rate. For intubated subjects in particular, sedative, pain, anesthetic, and/or anti-anxiety medications that are frequently required should only be used to the extent they are needed for those reasons, and not to control blood pressure in place of nicardipine. *(continued on page 5)*

Friendly Reminders *(continued)*

A word about primary treatment failure:

To prevent your ATACH-II subjects from being labeled with ***"primary treatment failure",*** SBP must be lowered to the assigned range within two hours of randomization. Important things to remember are to treat SBP as early as possible, randomize as soon as you are able to so the range is known, and then follow the titration schedule closely. Additionally, **pay attention to when and how subjects are transferred,** and encourage SBP control and careful monitoring of SBP as effectively as possible during transfers if they can't be avoided during the initial two hours. The most common reason heard for **preventable** primary treatment failure is subject transfer from the ED area to the ICU during this critical time.

Assistance in speaking with your site pharmacist or working through nicardipine-related concerns is always available. Remember to use the atachstudydrug@gmail.com email address for help with initial supply or re-ordering of study nicardipine for ATACH-II. Urgent questions should go to the hotline, where Dr. Qureshi or an experienced study physician is always close at hand to provide expert clinical advice. Calls to the hotline about nicardipine use in ATACH-II have included resolving complex cross-reactivity for a subject with other drug allergies before making an enrollment decision, and a wide variety of questions about starting, stopping, and titrating nicardipine correctly under many other diverse circumstances.

Getting to Know the ATACH-II Team - Meet Kristina Hill

Kristina Hill is the Data Manager at the Medical University of South Carolina

Where did you grow up?
Half outside the US, and half a small town in NW GA, USA.

What is the best advice you've ever received?
Be kind; everyone you meet is fighting a battle you know nothing about.

If you could travel anywhere, where would you like to go?
Anywhere I've never been! South America is next on my list.

What is one of your favorite habits?
Going running early in the morning when the world is quiet.

Do you like to plan things out in detail or be spontaneous?
Incurable planner, but I can act on the spur of the moment if I need to!

2015 ATACH-II Investigators' Meeting Pictures

Dear Logan -
Letters about Imaging Procedure

Dear Readers,

I regret to inform you that this will be my last column. I am leaving the ATACH-II trial on April 30th as I will be starting medical school this summer. I have had such a wonderful time working for the study and working with all of you. The people I have met along the way have all been kind and helpful and I don't know if I would have been able to accomplish my goals without their support. To my readers, I would like to thank you for all of your support as well. All of your help with the imaging process has made my job so much easier and I am happy with the contribution our images have made to both the ATACH-II trial and all the other studies involved. I believe the efforts we have put into this trial will translate into better care for stroke patients and I am proud to have been a part of it.

Thank you all again for the wonderful couple of years I have spent with the study. Your dedication towards advancing medical care and working tirelessly for your patients has been an inspiration and I look forward to taking this inspiration and applying it within my own practice someday.

Sincerely,

Logan Brau

Please welcome Rauf Afzal who is replacing Logan and continue to send all ATACH-II images to:

Attention: **ATACH-II Research**
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925 Delaware Street SE, Suite 300
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Recent DSMB Meetings

February 23, 2015
The DSMB found everything to be satisfactory and recommended that the study proceed as planned.

May 6, 2014
DSMB had no safety concerns and recommended that the study continue as planned.

November 1, 2013
The DSMB recommended to NINDS that Clevidipine not be allowed as an alternative to Nicardipine for the ATACH-II trial.

October 6, 2013
DSMB had no safety concerns and recommended the study continue.

April 22, 2013
DSMB reviewed the safety and overall progress of the trial: found everything to be satisfactory and recommended the study proceed as planned.

The next DSMB meeting will be in six months.

The Current Contact Information for ATACH-II

Don't hesitate to reach out to us - we are here to help you!

Need help with an enrollment or other urgent ATACH-II need?

Call the Toll Free Hotline at: 1-855-870-7205 *or* 952-225-0779
The hotline service will ensure that you are connected with a core team member who is available to help you immediately.

General Questions? Contact Kathy France at 612-625-6974 or kafrance@umn.edu

Contract or Reimbursement Questions? Contact Jessy Thomas at 612-624-2431 or thoma098@umn.edu

WebDCU Questions? Contact Cassidy Conner at 843-876-1105 or connerc@musc.edu

NETT CCC Questions? Contact 734-232-2142 **or** ATACHII-TRIAL@UMICH.EDU

Study Drug Questions? Please email your questions or requests for additional study drug to atachstudydrug@gmail.com

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Funded by NIH through grants U01NS062091 and R01NS061861; The content is solely the responsibility of the authors and does not necessarily represent the official views of NINDS or NIH.