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Miami VA Research & Development

BRUCE W. CARTER
DEPARTMENT OF VETERANS AFFAIRS
MEDICAL CENTER

Inside this issue:

Miami VA Received Full AAHRPP Accreditation

The VA took a national leadership role when, in 1999, Dr. Kenneth Kizer, then Undersecretary of Health, Department of Veterans Affairs outlined the VA's plans to seek an external entity to serve as an accrediting body for its research programs thus developing and setting the standards for an accreditation process for human research programs. Dr. Kizer outlined the accreditation processed that existed at that time for both accreditation of hospitals as well as for animal research facilities. He pointed out that there existed no comparable mechanism for accreditation of human research protection programs. Today over 90 VA facilities hold accreditation of their HRPPs (either NCQA or AAHRPP) and nationwide more than 129 organizations representing 550 entities have received AAHRPP accreditation.

The Miami VA achieved its first accreditation from the National Association for Quality Assurance (NCQA) on November 21, 2005, which was valid for three years. The VA subsequently changed accrediting bodies and re-accreditation of its components is conducted by The Association for Accreditation of Human Research Protection Programs, Inc. (AAHRPP).

A multiple-disciplinary group was organized that included representatives of Research and Pharmacy as well as Compliance Office personnel who worked long months in preparing for the re-accreditation process. The Miami VAHCS underwent a site visit as part of the re-accreditation process on August 7th and 8th. Visitors interviewed selected Principal Investigators, their study coordinators, members of the hospital's Institutional Review Board (IRB) as well as Leadership and Research Service personnel. A draft report was presented to the facility on September 5, 2008 and a response was submitted to AAHRPP on October 5, 2008. The Council on Accreditation met on December 11th and 12th and awarded full accreditation to the Miami VA.

Novartis Open House

On October 10, 2008, the South Florida VA Foundation for Research and Education hosted a very successful Open House for Novartis Pharmaceutical Corporation. 12 Novartis Representatives ranging from a National Director, Regional Science Directors and Clinical Research Associates presented current and upcoming research information to Miami's scientific community. Ample time was given to 20 VA investigators and research staff to meet and network with representatives from almost every therapeutic area. Novartis was given contact information from interested Investigators to promote the firm commitment to collaborate on research endeavors.

In early November, Novartis contacted the SFVAFRE about the new clinical trial entitled "A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II – IV)".

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PRIM&R IRB 250

On October 17, 2008, the Miami VA in collaboration with the Miller School of Medicine hosted its second annual PRIM&R Institutional Review Board (IRB) 250 Workshop. The IRB 250 is a topic-specific educational program that has been customized to the interests and needs of the Miami VA Healthcare System. The full-day program began with a discussion on the Criteria for the Review of Research followed by four modules that included: **Unanticipated Problems and Adverse Events, Conflict of Interest, IND and IDE: Requirements and the IRB and Informed Consent**

The speakers this year were Dr. Jeffrey Cohen, President of HRP Associates, Inc., and Dr. Ernest D. Prentice, Associate Vice Chancellor for Academic Affairs at the University of Nebraska Medical Center (UNMC). 127 participants attended the workshop. The instructional material distributed included copies of the speakers' presentations and the updated IRB Resource Guide. If you are interested in receiving an electronic version of these documents, please send your request to iperez4@med.miami.edu. The feedback from the participants has been very positive and the workshop has proven to be a valuable educational activity which the VA hopes to continue to host annually.

For those who were unable to attend the 2008 PRIM&R IRB 250 Workshop, we hope to see you next year.

Research Highlights

Telemedicine: *Bernard Roos and Herman Cheung are collaborators on a new automated system that would allow patients to monitor their health and report symptoms via cell phones and home telephones*

Researchers Collaborate On New Automated Health Monitoring System

In a less-expensive form of telemedicine, patients with asthma, diabetes, and other serious medical conditions will soon be able to report their health status and symptoms to physicians and nurses by accessing a form of technology owned and used by millions of people everyday: a telephone.

A new automated, interactive voice-recognition system, developed by researchers from the University of Miami's College of Engineering and Miller School of Medicine, would make automated telephone calls to patients everyday, employing prerecorded scripts to check up on whether they are experiencing breathing problems, fluctuations in weight, or any of a host of other health conditions.

"The goal is to get patients to be more proactive about their health," says Herman Cheung, the James L. Knight Chair and Professor of Biomedical Engineering at UM who helped develop the system. "They can use their phones to report information about their health and manage their disease."

Here's how it would work:

Patients who sign up for the service would get an automated call to their cell or home phone each day, and depending on what condition they have, would be read a script of health-related questions to which they would give either a yes or no answer.

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Hermes Florez, MD, MPH, PhD

GRECC Associate Clinical Director
Miami VA Healthcare System
Associate Professor of Clinical Medicine & Epidemiology
Divisions of Endocrinology & Geriatric Medicine
University of Miami Miller School of Medicine

In November during the month of diabetes awareness, prevention and management, Dr. Hermes Florez was honored by being one of eight US faculty/scientist invited to speak in the "Best of the American Diabetes Association (ADA) in India" (Nov 6-11, 2008). This is a program supported by the ADA to educate providers in India on hot topics to improve the quality of care of patients with diabetes in India. Speakers were chosen among those that presented conferences in this year ADA scientific session and ADA advance postgraduate course in San Francisco. India leads the world in the number of patients with diabetes (40 million), which are expected to double by year 2030. The topics that Dr. Florez spoke about were 1) Diabetes Prevention: Strategies for Implementation, and 2) Management of Diabetes in the Elderly.

Dr. Florez believes that sharing experiences at the University of Miami Miller School of Medicine in the US Diabetes Prevention Program (DPP) as well as the implementation of DPP strategies in Latin American countries, such as Venezuela and Chile, may provide a framework to halt the epidemic of diabetes in India and other countries. In addition, there are challenges and lessons learned to provide appropriate care to older adults with diabetes, particularly in view of recent data from the Veterans Affairs Diabetes Trial and other national and international studies. The strategy to prevent chronic complications, promote healthy aging, and preserve quality of life in elderly diabetics involves lifestyle intervention (diet and exercise), appropriate management of blood pressure, lipid abnormalities and glycemic control, as well as proper screening and management of geriatric syndromes (cognitive decline, depression, falls, urinary incontinence, polypharmacy, and frailty).

In the News

Intensive Glucose Control Provides Little Benefit to Eyes and Renal Outcomes in Older Diabetics

ROME (EGMN) - Eye and renal complications were no less frequent in older, difficult-to-treat patients with type 2 diabetes who were randomized to intensive rather than standard glucose control in the Veterans Affairs Diabetes Trial. Furthermore, there was no difference between the two treatment approaches in the development of any new diabetic neuropathy, according to results presented on Sept. 10 at the annual meeting of the European Association for the Study of Diabetes. These latest findings from the 7.5-year trial followed on from the primary end point data presented at the American Diabetes Association meeting in May 2008 just 8 days after the trial had ended. The latter showed that there was no difference between intensive and standard lowering of glycated hemoglobin A_{1c} (HbA_{1c}) in terms of overall cardiovascular protection. The two cochairs of the Veterans Affairs Diabetes Trial (VADT) - Dr. William C. Duckworth, of the Veterans Affairs Medical Center in Phoenix, and Dr. Carlos Abraira of the Miami Veterans Affairs Medical Center - discussed the new secondary outcomes data. Compared with standard glucose control, the intensive approach was associated with nonsignificant differences in the number of new eye procedures, which included cataract surgery (10.2% vs. 11.6%),

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Carlos Abraira, M.D.

CoChair, VA Diabetes Trial (VADT, CSP#465)

Professor of Medicine-VAMC, U. of Miami Miller School of Medicine

In the News

The **Division of Gerontology and Geriatric Medicine** has recently hired two new Assistant Professors who will be affiliated with the Miami GRECC. Dr. Priya Rai and Dr. Ramiro Verdun bring expertise to Miami that will significantly expand our capabilities to engage in aging research, particularly in the fields of reactive oxygen species, DNA damage, and telomeres.

Drs. Roos, Levis, Florez, and Troen from the Miami GRECC are working to establish a longitudinal study of aging in collaboration with the UM and FAU. They are working closely with Dr. Joseph Ouslander and others.

Dr. Troen recently visited the Center on Aging at the University of Florida in Gainesville and gave a presentation entitled "Vitamin D: Skeletal Health and Beyond (a stealthy epidemic)". It was an opportunity to also meet and talk with a number of investigators and potential collaborators, including Drs. Marco Pahor, Christy Carter, and Christiaan Leeuwenburgh.

Dr. Troen also recently attended a Longevity Consortium Symposium in Washington, D.C. The Longevity Consortium is funded by a grant from the National Institute on Aging and seeks to bring together scientists to learn about the state-of-the-art of longevity research and develop new collaborations. Members of the Consortium engage in three types of research efforts:

1. Laboratories devoted to the identification of longevity-related genes and pathways in non-human species;

2. Studies of special populations (e.g., centenarians) that are engaged in the discovery of genes associated with longevity; and

3. Established longitudinal cohorts of elderly men and women that have DNA and excellent phenotyping that can be used to study candidate genes.

Research Highlights–Drs. Roos & Cheung *(continued)*

The system would also alert patients to take their medications or perform other prescribed daily routines such as testing their blood pressure or blood glucose levels.

Using data mining technology, the system would also record and store information entered by patients, and a built-in fail-safe feature, triggered by an answer that indicates a potential health problem, would immediately route the patient to an on-call nursing service or physician.

"The key elements that are delivered here are quality assurance and lower costs," says Bernard Ross, professor of medicine and director of the Division of Gerontology and Geriatric Medicine, who teamed with Cheung in creating the system. "We know how to manage diseases, but we don't have the communication to educate, to maintain the surveillance. So this automation process assures that the patient is taken care of according to best-practice guidelines."

According to Roos, the system will cover 80 percent of the five most common causes of disability and hospitalization, including congestive heart failure, hypertension and stroke, chronic obstructive lung disease, asthma, and diabetes.

Roos says about 70 percent of a nurse's time is spent monitoring the health of a patient. The system he and Cheung created automates that process, freeing up health care providers to take care of patients who need immediate help.

UM Innovation, which develops university-generated treatments or devices and works with businesses to take that technology into the marketplace, helped Cheung and Roos get a patent for their system.

The system could be on the market within two years, Cheung says, noting that the Miami-based company that partnered with them on its development, GenerationOne, "is already in very active negotiations with a number of large, national medical insurance groups" that would make the automated system available to patients.

Upcoming Events

The site visit for the review of the **Miami Institutional Animal Care and Use Committee (IACUC)** will take place on **January 6-8, 2009**. Ms. Mary Lou James, BA, LATg, Consultant, Regulatory Compliance Research Animal Welfare will conduct the review. The review is intended to provide helpful recommendation to the Research Office as well as to provide a summary report to VA Central Office following the final visit.

I A C U C Site Visit

January 6-8, 2009

We are pleased to announce that the

Fifth Annual Lawrence M. Fishman Visiting Professor In Endocrinology

is scheduled for **January 28-29, 2009**. In honor of his more than 40 years of service to the University of Miami and the Miami Veterans Administration Medical Center, this year's Fishman Professor is none other than Lawrence M. Fishman, M.D., FACP himself

Wednesday, Jan. 28, 2009	Thursday, Jan.29, 2009
Noon:	1:00 PM:
Medical Grand Rounds:	Endocrinology and Metabolism Clinical Conference
Medicine and the Arts	*'Electrocortin': Fifty+ Years On*

Novartis Open House *(continued)*

On November 13, Novartis conducted a site visit and Dr. Schob was selected to participate in the Novartis SPP100F2301 Heart Failure clinical trial.

Novartis Pharmaceutical Corporation has demonstrated a firm commitment to developing long term relationshiops with VA Investigators. The master CRADA they negotiated is intended to streamline participation in any clinical trial that VA Investigators would like to take part in with them. It is hoped that this will be the first in a series of Open Houses with pharmaceutical companies that have executed master CRADA's with the VA.

Research Investigators interested in participating in future studies can contact the SFVAFRE for further information.

Recent Publications

VA Investigators at the Miami GRECC

1. Cherniack, E.P., Troen, B.R. and Levis, S. Hypovitaminosis D in the elderly: from bone to brain. J Nutr Health Aging. 12 (6):366-73, 2008.

2. Duque, G. and Troen, B.R. Understanding the Mechanisms of Senile Osteoporosis: New Facts for a Major Geriatric Syndrome. J Am Geriatr Soc, 56:935-941, 2008.

3. Cherniack, E.P., Levis, S. and Troen, B.R. Hypovitaminosis D: a stealthy epidemic requiring treatment. Geriatrics 63(4):24-30, 2008.

4. Yang, G., Zaidi, M., Zhang, W., Zhu, L.L., Li, J., Iqbal, J., Varbanov, A., Gross, G., Phipps, R., Troen, B.R., Sun, L.. Functional grouping of osteoclast genes revealed through microarray analysis. Biochem Biophys Res Commun. 8;366(2):352-9, 2008.

5. Florez, H. and Troen, B.R. Fat and Inflammation: A Dual Path to Unfitness in Elderly People? J Am Geriatr Soc, 56(3):558-60, 2008.

6. Cherniack, E.P. and Troen, B.R. Calciotropic Hormones. In "Senile Osteoporosis: Advances in Pathophysiology and Therapeutic Approach" (Duque, G. and Kiel, D., Eds.) Springer-Verlag London Limited, pp. 34-46, 2008.

In The News- Dr. Carlos Abraira *(continued)*

"There were no differences in proliferative diabetic retinopathy or macular edema," said Dr. Abraira, and "no difference in new onset of retinopathy." However, he noted that slightly more patients in the intensive therapy arm, compared with the standard control arm, required laser eye surgery overall (8.3/100 patients per year vs. 7.5/100 patients per year). In addition, the percentage of patients who developed retinopathy early - defined as a two-step increase in the Early Treatment Diabetic Retinopathy Study scale - was marginally higher in the less intensively treated patients than in the intensively treated controls (22.1% vs. 17%). With regards to kidney complications, Dr. Abraira said that the decline in renal function was similar in both groups of patients, and severe renal disease - evidenced by doubling of serum creatinine, serum creatinine greater than 3 mg/dL, or end-stage renal disease - was "unaffected by glucose control." Having a prior cardiovascular event, being a smoker, or having microalbuminuria or retinopathy at baseline were expected predictors of progression to macroalbuminuria, said Dr. Abraira. While progression from normal or microalbuminuria to overt proteinuria did not differ between standard and intensive glucose control, there was a significant decrease in progression from normal to micro- or macroalbuminuria in the intensively treated patients (31% vs. 38% for standard control, $P = .02$). Dr. Abraira also showed that the percentage of patients in the standard vs. intensive treatment arms with neuropathy was similar: any neuropathy, 43.8% vs. 43.5%; mononeuropathy, 4% vs. 4.7%; and peripheral neuropathy, 40% vs. 38.4%. However, there was a slightly higher percentage of patients in the intensive glucose control arm that developed autonomic neuropathy (8.2% vs. 5.2%) though this was not significantly different. Dr. Duckworth pointed out that the 1,791 patients enrolled in the VADT were a difficult-to-treat group, with a mean age of 60 years and a median duration of diabetes of 11.5 years. The mean HbA_{1c} at the start of the trial was 9.4% and fell to a median of 8.4% in the standard glucose control arm and 6.9% in the intensive glucose control arm. Importantly, patients in the trial achieved good blood pressure control and "almost ideal" levels of LDL cholesterol and other lipids, Dr. Duckworth said. This suggests that in the presence of optimal risk factor management, it does little to add intensive glucose control in terms of the overall benefits that can be achieved. "The VADT investigators must be as disappointed as I am in realizing that strict glycemic control did not result in major differences in macrovascular complications," said Dr. Stefano Del Prato, of the University of Pisa (Italy), referring to the lack of benefit in preventing diabetic retinopathy, nephropathy, and neuropathy.

IMPORTANT NOTE from the

Department of Veterans Affairs
Office of Public Affairs

Physician/Research Publications:

Physician and Researchers are required by VA regulations to provide credit to VA in any publications or periodicals based on work conducted or funded by VA. When VA provides the major salary support for a research project, VA must be named first in the credit line of books, chapters, articles and abstracts. The credit line should include the physician's VA title, followed by Miami Veterans Affairs Healthcare System, Miami, FL. Physicians and researchers, who are at least a 0.5 FTEE for VA or are receiving 50% of their salary from VA, must acknowledge their VA affiliation. If VA provides no direct research funding, but the research involved the use of other VA resources (i.e. facilities or patients), VA credit must be listed in all publications. Failure to acknowledge VA support or employment may result in discontinuation of current VA Research and Development (R&D) Funding and/or ineligibility to receive future R&D funding for a period of up to five years.

***Susan E. Ward**, Public Affairs Officer*

SFVAFRE Corner.....CRADA's under negotiations

Investigator: **Seth Spector, M.D.**
Sponsor: Sanofi-aventis U.S., Inc
Title: *"Multicenter, Randomized, Double-Blind Study Comparing the Efficacy and Safety of AVE5026 with enoxaparin for the Primary Prevention of Venous Thromboembolism in Acutely Ill Medical Patients with Restricted Mobility"*

Investigator: **Alan Schob, M.D.**
Sponsor: Novartis Pharmaceuticals
Title:"*A multicenter, randomized, double-blind, parallel group, active-controlled study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure (NYHA Class II – IV).*"

Investigator: **Andrew Quartin, M.D.**
Sponsor: Bayer HealthCare Pharmaceuticals
Title:*"A Double-Blind, Placebo-Controlled, Randomized, Parallel-Group, Multicenter, Multinational Study to compare the Safety and Efficacy of Amikacin Pulmonary Delivery System (Amikacin Sulfate Solution for Inhalation and the Pulmonary Drug Delivery System [PDDS Clinical]) with Standard of Care in Intubated and Mechanically-Ventilated Patients with Gram- Negative Pneumonia*

Submission Calendar for All R&D Services

January	February	March	April
		BLRD / CSRD Proposal Due HSRD, RRD & CD Reviews	All services Career Dev (CD) LOI Cut-off for **June Proposals** RRD LOI Cut-off for **June Proposals**
May	**June**	**July**	**August**
HSRD Abstracts & Intent to Submit due **May 1**	All Services CD Proposals Due HSRD / RRD Proposal Due (Merit Review & NRI) BLRD and CSRD Reviews		
September	**October**	**November**	**December**
BLRD / CSRD Proposal Due HSRD, RRD & CD Reviews	All services CD LOI Cut-off for Dec. Proposals RRD LOI Cut-off for **Dec. Proposals**	HSRD Abstracts & Intent to Submit due **Nov 3**	All Services CD Proposals Due HSRD / RRD Proposal Due (Merit Review & NRI) BLRD and CSRD Reviews

All due dates are the 15th of the month and will adhere to this calendar, unless specifically announced in an RFP.

FEEDBACK

Faculty and staff submissions should be e-mailed to the Office of Research Communications at

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