



Miller School Comprehensive Diabetes Center Concludes Clinical Drug Trials

The University of Miami Miller School of Medicine participated in the Glycemia Reduction Approaches in Diabetes (GRADE) – A Comparative Effectiveness multi-center clinical trial, marking the end of a 10-year effort aimed at finding the most effective medications for treating Type 2 diabetes.



Rajesh Garg, M.D.

The study began in 2011 in response to limited information of diabetes treatment effectiveness in the U.S., particularly among minorities diagnosed with the disease. Previous studies supporting GRADE showed a rise in obesity as well as that Black and Hispanic populations are 50% more likely to have diabetes than non-Hispanic white people.

GRADE Origins



With funding from the National Institutes of Health and the U.S. Department of Veterans Affairs (VA), and in partnership with the American Diabetes Association, the Miller School was one of 37 centers in the country – and the only one in Florida – selected to recruit and test various FDA-approved medications for their effectiveness in the treatment of Type 2 diabetes.

The recruitment and management of the Veterans in Miami site was very successful (one of the tops in the study) with support from Willy Valencia, M.D., Violet Lagari, M.D., M.P.H., and other investigators at the Miami VA Healthcare System, which includes the William "Bill" Kling VA Clinic in Sunrise and the Bruce W. Carter VA Medical Center in Miami.

“This study featured a collaboration between UM and various South Florida Veterans Affairs,” said Rajesh Garg, M.D., professor of medicine at the Miller School and Director of the Comprehensive Diabetes Center at the University of Miami Health System. “The study had 5,000 total patients with the Miami Center recruiting nearly 200 participants in South Florida.”

Jennifer Marks, M.D., former Miller School professor and previous chief of endocrinology, diabetes, and metabolism, led the early planning stages as co-PI. Hermes Florez, M.D., Ph.D., former Miami Geriatric Research, Education and Clinical Center (GRECC) Director and Miller school professor, and current Associate Dean for Population Health and chair of the Department of Public Health Sciences at the Medical University of South Carolina, served as the other PI at the Miami VA and then at the Miller School from 2013–2020.

“Miami was a great fit as a center for this study due to its



diversity and proven track record of previous successful recruitment for medical studies,” Dr. Florez said. “Florida also provides a great advantage in having a population of older adults that were vital to the study.”

Trials in Action



Hermes Florez,
M.D., Ph.D.

After the two-year planning period, patient recruitment started in 2013 and continued to 2017. Participants were screened and assessed by the Miller School with criteria including those having Type 2 diabetes with a narrow hemoglobin A1C range; those on treatment with metformin; and patients with less than 10 years of having the disease. Nationally, 5,000 patients were selected with a patient population consisting of 20% Black and 18% Latino and with an average age of 57.

Interested participants who met the criteria were divided into four groups and given a single medication out of the four. Medications consisted of two injectables (liraglutide and



insulin glargine) and two in tablet form (glimepiride and sitagliptin).

Patients received the single medication along with the drug metformin, and progress was checked every few months at the clinics for an average of five years. Clinical supervision consisted of in-person and telehealth visits during the COVID-19 pandemic with blood collection kits sent to the central lab for testing following the study's uniform protocols.

"This was perhaps one of the biggest challenges in getting the patients and continuing getting the information in a timely manner," Dr. Garg said. "It was a big effort in following the patients over time, but thankfully we have a group of coordinators, data analysts, administrative support, and three doctors always working on the study."

Lessons Learned

The results of the GRADE study were presented at the Scientific Sessions of the American Diabetes Association (ADA) meeting showing that the drugs liraglutide and insulin glargine were the most effective of the four medications in keeping A1C levels below 7%.

The drug glimepiride had a lesser effect, and sitagliptin showed the lowest impact, resulting in the highest frequency of participants developing A1C levels greater than 7%. Insulin glargine was most effective in keeping A1C levels less than 7.5%, a secondary outcome of the study. The results were similar among men and women and across different race, ethnic, and age groups.



“This trial has shown that while many medications are available, not all are the same,” Dr. Garg said. “We had to decide which is best, and this study helps us while having a significant impact on the way we treat diabetes in a market where \$9 billion to \$10 billion worth of these drugs are sold every year.”

Patients involved in the trial were given a profile of their study analyzing their responses to their specific medication over the years. Patients wish to explore other drug options can discuss them with their primary care provider as desired.

“Preliminary results also showed potential benefit of liraglutide reducing the risk for cardiovascular disease and hospital admission for heart failure” Dr. Florez said. “Future follow-up of the GRADE study participants can provide additional information on the cardiovascular benefits and even bone health benefits associated with this medication.”

The next chapter in the study begins by analyzing the years’ worth of data. Performing cost analysis of the medications, publishing papers, remote studies, and even monitoring the patients used in the trials will serve as critical points moving forward.

“It’s significant work because it was a great national effort,” Dr. Garg said. “Because ours was the only center chosen in Florida, it becomes essential that we contribute to studies like this and do it well. This will have long term implications on how we are going to manage future treatment of Type 2 diabetes.”



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