Study Protocol

Official Title: Remission through Early Monitored Insulin Therapy - Duration Month (REMIT-DM)

ClinicalTrials.gov ID (NCT number): NCT03670641

Protocol Date: 06 July 2021

Scientific Background

REMIT-DM is a feasibility study that aims to show that previously published diabetes remission through early use and titration of short-term insulin therapy is possible and safe in the ambulatory diverse American population of patients with T2D, with continuous glucose level and trend information provided by CGM. We developed the algorithm based on published diabetes remission studies and include within the algorithm the CGM trend arrows to further refine insulin doses for both safety and efficacy purposes. Data captured by the CGM transmits automatically to the cloud and is accessible at any time of day by the multidisciplinary diabetes team, which includes the certified diabetes educator (CDE) and Endocrinologist. The CGM-guided insulin titration algorithm is designed to achieve euglycemia (defined as fasting CBG < 100 mg/dL, and 2 hour post-prandial CBG < 120 mg/dL) within 2 weeks of initiating insulin therapy, then to help maintain euglycemia for 2 weeks before discontinuing insulin entirely. Ten subjects will undergo a maximum of 4 weeks of insulin therapy and will be assessed for remission afterwards to confirm enough recovery of beta cell function. (Complete remission is defined as fasting glycemia <100 mg/dL without use of pharmacological therapy.) Afterwards, we will implement American Diabetes Association (ADA) guidelines for standard glycemic management, as necessary. We will use the data collected during this feasibility study to sharpen the CGM-guided insulin titration algorithm for creation of a T2DM remission mobile application that could then be tested and studied in a larger sample size.
The feasibility study will also take into account clinically meaningful data points e.g. the number of phone calls between the patient and the diabetes team, the patient experience, and patient satisfaction.
Study Objectives

Study Design & Methods

Participants will be assessed by the endocrinologist and diabetes educator to be able to perform skills necessary for CGM use and insulin delivery. If the CDE determines that the patient is unable or unwilling to perform the necessary care tasks, this will be communicated to the endocrinologist for potential exclusion from the study.

The Research Activities:

-Study Visit 1: The PAID-5 survey will be administered to assess diabetes distress by the RN CDE prior to the diabetes education session. Subject will undergo standard of care diabetes self-management education by the study team members, including the initiation of the CGM. OGTT lab blood draw will be done.

-Study Visit 2: Subject will undergo standard of care education for insulin start. Research activity: study team will provide the insulins and instruct the subject in the insulin titration protocol and how CGM readings will be used to manage insulin doses. Subject will adjust their meal-time insulin doses by the before meal blood sugar and the CGM predictive arrows and their daily basal insulin based on how close fasting glucose was to glucose target. Study team will confirm that subject understands how the study works using the teach-back method. Ample time for question and answer will be allotted.

-Study Visit 3: The PAID-5 will be administered at this visit as well as the satisfaction survey. These will both be administered by the RN CDE prior to the education session. If remission is achieved, patient will turn in their CGM and go off their insulin. A repeat OGTT lab blood draw will be done at this time as well. If remission is not achieved, the standard ADA algorithm would apply and patient would be placed back on their medication(s). However, there may be some patients that would prefer to stay on insulin or for which remaining on insulin therapy is

appropriate. The patient will be started on appropriate therapy as guided by clinical decision making.

-Study Visits 4-6: post 4 weeks-1 year patient will have standard of care endocrinology visits driven by clinical decision making.

-Study Visit 7: At 12 months, the PAID-5 and satisfaction survey will again be administered by the RN CDE.

Algorithm Development/Data Analysis Period:

-Post 12 month intervention period: Algorithm and Protocol development

All program data, e.g. number of calls, length of calls, information reviewed/requested on call, documentation of extraneous calls, e.g. after hours/outside of schedule. Clinical outcomes, e.g. rates of hypoglycemia, laboratory results will be analyzed and reviewed. Based on the findings a full protocol that includes the finalized insulin titration algorithm and program processes will be prepared.

Eligibility Criteria

Inclusion criteria:

- Age ≥18
- A1C criteria - >7.0
- Diagnosed with T2D within 4 years
- Lifestyle controlled
- Subject may be on up to 2 medications for diabetes.
- Smart phone or home computer compatible with DEXCOM CLARITY software
- English speaking
- Assessed by endocrinologist and diabetes educator to be able to perform skills necessary for CGM use and insulin delivery

Exclusion criteria:

- Autoimmune Type 1 DM, defined as positive GAD65 or islet cell antibodies
- Pregnant
- Chronic Kidney Disease (CKD) Stage IV or greater
- Mental and/or cognitive disorder (based on documented disorder and/or assessment of physician or educator)
- No access to computer for downloading CGM
- BMI <18.0

Statistical Considerations

This is a feasibility study that does not require power calculation.

Baseline characteristics will be described using measures of central tendencies (means, median, standard deviations). To examine time to glucose target range, hypo/and hyperglycemia, logistic regression will be used. Covariates in the models will include demographic factors, glucose dosing information, insulin protocol used.