Study Protocol

Full Title	**"Transition of T1DM patients aged over 65 years into AHCL (780G) insulin pump: the impact on glucose patterns, quality of life physical & cognitive measures, as well as vascular status"**
Short Title	AHCL insulin pump in older patients
Protocol No	1.0
version	3.0
Release date	08 June 2022
Type of study	A two-centers, randomized controlled, parallel group study.
Clinicaltrials.gov #	Will be filled after registration of the study
Sponsor name and address:	Prof. Tomasz Klupa
Trial Coordinating Investigator name	Prof. Tomasz Klupa
Trial Coordinating Investigator contact details	Prof. Tomasz Klupa Jagiellonian University Medical College, Jakubowskiego 2 30-688 Kraków, Poland Tomasz.klupa@uj.edu.pl 48 697 40 30 40
Participating sites and investigators	Jagiellonian University Medical College, Poland
Device under investigation	MiniMed™ 780G Advanced Hybrid Closed Loop (AHCL))

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1. BACKGROUND OF THE STUDY

Recent advances in insulin pumps, continuous glucose monitoring (CGM) devices, and control algorithms have resulted in an acceleration of progress in the development of the automated systems of insulin delivery including advanced hybrid closed loop (HCL) insulin pumps. The results of the AHCL insulin pump based studies published so far are very encouraging, including that Medtronic-sponsored study performed at our center "Transition of CSII/CGM naïve patients directly into AHCL (780G) insulin pump: the impact on glucose patterns and quality of life measures" (1-6). Unfortunately there is little data concerning the usage of AHCL systems in older patients. The management of these individuals is particularly challenging as older adults with type 1 diabetes are especially vulnerable to hypoglycaemia. The recent ADA/EASD consensus underlines that the use of advanced technologies in older individuals is useful and should not be discontinued or a priori excluded because of the older age (7). Since the AHCL systems are very effective in hypoglycemia prevention they could be considered the treatment of choice in older patients with T1DM. The open question is how effectively would older individuals adopt this advanced technology, how would they accept it, and if the simplicity in terms of everyday usage of AHCL versus less advanced technologies would be appreciated by older individuals with T1DM. Older people with diabetes have a higher risk for cognitive impairment and for physical disability whether this may be effected by an improvement in glucose indices is unknown. Thus, the aim of this study is to assess the efficacy of AHCL in people with type 1 diabetes in improving glucose indices, quality of life and physical capacity indices.

2. TRIAL DESIGN

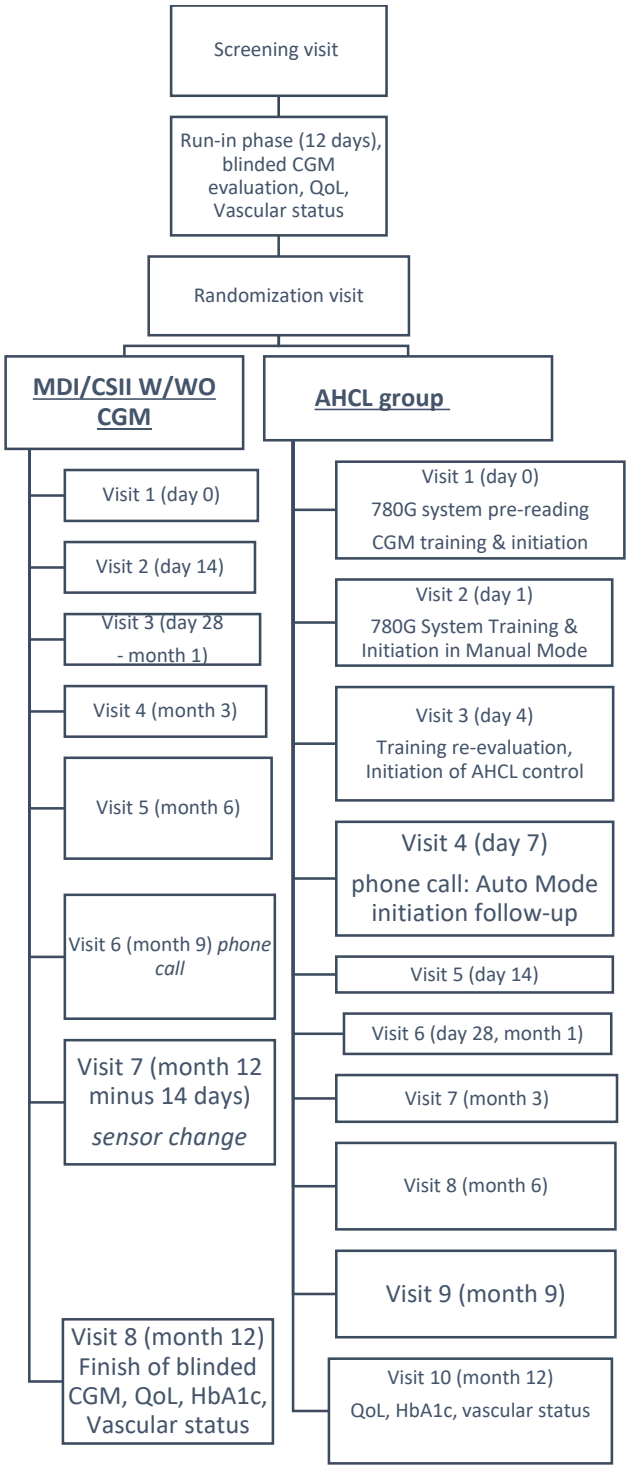
2.1. Objectives

The primary objective of this study is to evaluate whether the AHCL (MiniMed 780G®) system improves glycemic control and quality of life in older (above 65 years of age) individuals with withT1D and if one year ACHL treatment may affect vascular improve of those patients.

2.2. Study design

The trial is a two-centers, randomized controlled, parallel group study. Patients will be followed up during approximatively 12 months, with preliminary evaluation concerning efficacy and safety performed at 6 months.

Figure 1: Study Design



2.3. Visits and Procedures

2.3.1. Run-in Phase

Screening visit:

- Patients' eligibility assessment,
- obtaining of informed consent,
- QoL questionnaire, the WHO-5 questionnaire as well as the General Heath question will be used
- lab tests: HbA1c, eGFR, ASPAT, TSH
- Vascular status : Intima-media thickness-IMT, Flow-Mediated Dilatation -FMD and Laser Doppler Flowmetry- LDF.
- Sarcopenia/functional status/frailty will be assessed using several tools:

1) Well validated tests of balance, strength & aerobic capacity. This will include:

   Gait, Balance & Aerobic Capacity Measurement

   The following instrument will be used to assess gait speed balance and aerobic capacity

   Timed up and Go[1] [2-4]

   The objective of this test is to measure the ability of a person to: stand up, walk, turn around and sit down safely in a timely manner. The test examines most mobility skills. The participant is told to get up from a chair with handles, walks 3 meters, turns, walks back, and sit down again. The score is according to the length of time in seconds to complete the task. The score is categorized according to the risk for falls and independent walking. The following cut-offs are conventionally used: less than14 seconds = independent mobility; 15-20 seconds= semi-independent mobility may have a some what increased risk for falls & needs further evaluation some may need a walking aid; 20-30 seconds= dependent mobility: need help walking, 50% with a cane, 40% walker, 10% supervision. Some will need help in transfers, and most will require help using the toilet. Many in this category won't go outside the home alone. Data suggests that the timed "Up & Go" test is a reliable and valid test for quantifying functional mobility that may also be useful in following clinical change over time.

   6 min walk[1,5-7]The six-minute walk test (6MWT) measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is allowed to self-pace and rest as needed as they traverse back and forth along a marked walkway. The six minute walk distance in healthy adults has been reported to range from 400m to 700m. People with lower vs. higher scores on the 6 minute walk are at higher risk for falls, disability, frailty, hospitalization and death.

   10 meter walk[8]: The test examines the pace and number of steps it takes a person to pass 10 meters. A route of 10 meters is marked by two lines and a chair is placed two meters past the runway end line. The subject starts the test two meters before the runway and goes 14 meters (two meters for acceleration at the beginning and two meters for deceleration at the end). The score achieved is determined by the time lapsed by the participant during walking along the middle 10 meters. Subject performs the test four times, the first two times are for practice: measurement occurs only during the third and fourths time. In addition to measuring the speed, the number of steps required to cross the short distance are also

counted. Studies have a shown that better gait speed is associated with a lower risk for functional decline, hospitalization and mortality.[9,10]

Berg Balance Scale (BBS): The berg balance test includes 14 tasks which evaluate static and dynamic balance. Each task receives a score of 0 to 4 points - depending on the quality and task execution time.[40-42] The maximum score is 56 points. The scores are dichotomized in the following manner:

1. Scores below 36 indicate impairment with an increased risk for falls.
2. Scores between 37-45 indicate need for a walking aid in order to walk in a safe manner.
3. Scores above 45 indicate an independent walker without an increased risk of falls.

The equipment used for the Berg balance test is a step stool, a mat table, a chair with arms, a tape measure, a stopwatch, a pen, and a table. Studies have shown that individuals with scores indicating impaired balance are at increased risk of falls resulting in hospitalizations and deaths.[11]

Four Square Step Test (FSST) [12]

The test evaluates dynamic balance in a high functional level and features walk forward backwards left and right above 2 90 cm and 2.5 cm high long sticks that divid the floor into four squares. The participant is stands in square 1 facing no. 2 square. The goal is to walk as quickly as possible in all the squares in the following order: from 1 to- 2,3,4,1,4,3,2 and 1 without touching the sticks. The score is the time required to complete the entire route.

Grip Strength

The maximum grip strength is examined utilizing the Jammer dynamometer. The test is conducted in a neutral hand position and repeated three times. The score is the average strength in kg this is compared to the general population according to age and gender.[43-46]

30 second chair stand.

The purpose of this test is to assess lower body strength. The participant is required to rise from sitting position with arms crossed as many times as possible in 30 seconds. Scoring is according to the number of stand executed in 30 seconds.[47]

Fried Scale

Frailty is defined as the presence of at list three components.[34]

i. Weight loss: “In the last year have you lost more than 10 pounds unintentionally (not due to dieting or exercise)?
ii. Poor endurance and energy: as indicated by self-report of exhaustion. Self-report exhaustion, identified by two questions from the CES-D scale.
iii. Low Physical Activity level: kilocalories expended per week, calculated adjusted according to age and gender.
iv. Walk time: over seven seconds to pass three meters

2) Participants will be asked to install an app developed in-house for the assessment of clinical sarcopenia in older people with diabetes (EFSD grant).

- Cognitive function will be assessed at baseline using the Montreal Cognitive Assessment (MOCA)[13] and a digital version of the Digital Symbol Substitution Test (DSST)[14]

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Run-in phase:

- Patient continues MDI/CSII treatment as per routine procedures
- The patient will be instructed to perform ≥ 4 blood glucose (BG) measurements per day
- Blinded CGM evaluation is performed for 12 days.

Randomization visit:

- BG meter data download, data review and optimization of MDI/CSII management.
- Blinded CGM data download.
- Patients will be randomized to either:
  - MiniMed 780G AHCL system, also referred to AHCL group
  - MDI/CSII

Randomization will be done by Random Allocation Software to allow fair distribution among sites and eliminate place for bias. http://random-allocation-software.software.informer.com/2.0/

2.3.2. Study phase

Both groups will have a similar number of visits in order to minimize bias. However, the AHCL group will have 2 additional visits to allow for patients to be trained on the AHCL system.

MDI/CSII group:

The patient continues MDI/CSII treatment as per routine procedures

- Visit 1 (day 0, can be combined with the randomization visit): BG meter data download, data review and optimization of MDI management.
- Visit 2 (Visit 1 + 14 days, window +/- 3 days): BG meter data download, data review and optimization of MDI management
- Visit 3 (Visit 2 + 14 days, window +/- 3 days – month 1): BG meter data download, data review and optimization of MDI/CSII management
- Visit 4 (month 3): BG meter data download, data review and optimization of MDI/CSII management
- Visit 5 (month 6*):* BG meter data download, data review and optimization of MDI/CSII management, blinded CGM evaluation start. Preliminary evaluation
- Visit 6 *(*month 9*) – phone call*
- Visit 7 (month 12 minus 14 days) - *phone call:* blinded CGM - sensor change.
- Visit 8 (Visit 6 + 6 days, window +/- 1 day): QoL questionnaire, blood sample for HbA1c lab test, blinded CGM data download, . vascular status : Intima-media thickness-IMT, Flow-Mediated Dilatation -FMD and Laser Doppler Flowmetry- LDF.
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Study conclusion.

AHCL group:

- Visit 1 (day 0, can be combined with the randomization visit): the patient will get the pre-reading materials on the 780G system, to be read before Visit 2. CGM training and initiation.
- Visit 2 (Visit 1 + 1 day, window +7 days): 780G system training and initiation in Manual Mode.
- Visit 3 (Visit 2 +3 days, window +3 days): 780G system data download. Auto Mode readiness assessment. 780G system initiation in Auto Mode with AHCL control
- Visit 4 (Visit 3 + 3 days, window +1 day) – phone call: Auto Mode initiation follow-up.
- Visit 5 (Visit 4 + 7 days, window +/- 3 days): 780G system data download, therapy assessment and optimization
- Visit 6 (Visit 5 + 14 days, window +/- 3 days, month 1): 780G system data download, therapy assessment and optimization
- Visit 7 (month 3): 780G system data download, therapy assessment and optimization
- Visit 8 (month 6): 780G system data download, therapy assessment and optimization. Preliminary evaluation of efficacy and safety (see primary and secondary endpoints except for vascular status assessment)
- Visit 9 (month 9):
- Visit 10 (month 12): 780G system data download, QoL questionnaire, blood sample for HbA1c lab test, vascular status : Intima-media thickness-IMT, Flow-Mediated Dilatation -FMD and Laser Doppler Flowmetry- LDF.
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  Study Conclusion

2.4. Inclusion criteria

1. Age over 65 years
2. T1DM
3. Willing to participate in a study for the specified duration
4. Willing to perform ≥ 4 finger stick blood glucose measurements daily

5. Willing to wear the system continuously throughout the study
6. Glycosylated hemoglobin (A1C) value less than 10.0% at time of screening visit
7. Treated with MDI/CSII (with exclusion of 780G)
8. Willing to perform at least 4 BGM/day, when on MDI/CSII
9. Lack of advanced complications of diabetes, eGFR>30

2.5. Exclusion criteria

1. Severe concurrent illness
2. Laboratory abnormalities, or medications that might affect study participation,
3. Severe renal impairment (eGFR<30)

4. hemoglobin A1c value above 10%
5. previous treatment with 780G

2.6. Study endpoints

Primary endpoint:

- Between group difference in the percentage of time spent within range with sensor glucose (SG) between 70–180 mg/dL (TIR) (3.9-10.0 mmol/L).

Secondary endpoints:

- Between groups difference in the percentage of participants achieving TIR >70%
- Between group difference in the percentage of time spent:
    - in hyperglycemic range with SG > 250 mg/dL (13.9 mmol/L)
    - in hyperglycemic range with SG > 180 mg/dL (10.0 mmol/L)
    - in hypoglycemic range with SG < 54 mg/dL (3.0 mmol/L)
    - in hypoglycemic range with SG < 70 mg/dL (3.9 mmol/L)

The above 4 endpoints will be also categorized by daytime (06:01 to 23:59) and night-time (00:00 to 06:00).

- Between group difference in the mean glucose level
- Between group difference in the glycemic variability measure by SD and CV
- Between group difference in the HbA1c levels
- Between group difference in the Diabetes Quality of Life (QoL) questionnaire score.

- Differences in baseline vs end of the study in vascular status as measured with IMT, FMD, LDF
- Difference in physical capacity indices listed in screening visit

Safety endpoints:

- Number of severe hypoglycemic episodes
- Number of DKA events
- Number of hospitalisations

2.7. Devices usage in the study

2.7.1. Run-in Phase

The Guardian™ Link 3 transmitter and Guardian™ Sensor 3 will be used in a blinded manner to collect CGM data for 2 weeks at baseline in all participants.The Guardian™ Link 3 transmitter will not be linked to a MiniMed™ pump, and therefore the sensor data will not be visible to the subject.

The data will be downloaded from the transmitter in the hospital to a computer by study team members, using a transmitter dock (Dock) and a specific software (Download Utility software). This data will not be used for therapy adjustment during the study. It will only be used for study data analysis.

2.7.2. MDI/CSII Group

Blinded CGM will be used at study end for 2 weeks to collect CGM data in the MDI/CSII group. The process will be the same as described for the run-in phase.

2.7.3. AHCL Group

In addition, patients from the AHCL group will use the MiniMed 780G AHCL system with Guardian™ Sensor 4.

The AHCL system will be initiated first in Manual Mode (i.e. without AHCL control) with suspend before low feature (Visit 1).

The validated protocol for SAP initiation, as previously described (8). In short, the protocol inputs the current insulin program (MDI) and calculates a 10–20% reduction in total daily dose, with a 40/60 basal/bolus distribution in four or five basal rates. Insulin-to-carbohydrate ratio (ICR) settings utilize the formula of 300–450/total daily dose (TDD) and the formula of 90–110/TDD (mmol/L) with two CF settings; the nighttime CF factor is set 10–20% higher than the daytime CF. Active insulin is set time (3 h); suspend before low feature is turned on with a threshold of 3.0–3.8 mmol/L (55–70 mg/dL), and glucose target ranges from 5.0 to 7.2 mmol/L (90–130 mg/dL.

The AHCL system will be initiated in Auto Mode (i.e. with AHCL control) at Visit 2 with the settings in the below table. The Insulin to Carb ratio (ICR) and the Active Insulin Time (AIT) may be adjusted by the physician during the study. The glucose target may not be adjusted, unless in case of safety concerns. The patients may not adjust system settings without consulting with the physician.

Basal insulin target of sensor glucose:	100 mg/dl
Insulin-Carb-Ratio:	Defined by the rule 500/TDD. TDD is the one observed during the period in Manual Mode
Active Insulin Time:	2.5 hours

At each visit, the AHCL system data will be downloaded and reviewed by the physician. The patient interaction with the system will be evaluated, included sensor calibration, bolus management (before the meals and for corrections as needed), alarms and Auto Mode exits.

At each visit, the glycemic control will be reviewed, and system settings re-assessed and adjusted as needed, including ICR, AIT and basal rates in Manual Mode.

2.8. Training process organization

2.8.1. Study staff training

Training of the Investigational Centers staff on the conduct of the study and the devices being used in the study will be performed before the protocol is implemented. All participating physicians, nurses and coordinators will be trained on the 780G system and the professional CGM. Specific Investigational

Center staff will be trained on each of the system's components. Training will contain both lecture and hands-on experience.

2.8.2. Patient training

At screening, all participants will be met by diabetes educator and dietician to verify their knowledge related to intensive, functional insulin therapy. Patients not meeting the requirements will not be eligible to pursue the study.

The patients randomized to the AHCL group will be trained both in the field of technical aspect of the usage of this technology and clinical aspects of the 780G based diabetes management. The successful training will be confirmed with 780G system Training Checklist developed by investigator.

This training will include basics on insulin pump therapy, such as basal/bolus concepts, blood glucose target ranges, and insulin sensitivity; and basics on pump features, including how to program the pump, how to use the Bolus Wizard calculator, the importance of using the Bolus Wizard for all meals and correction doses, and the use of infusion sets and reservoir management. The training will also cover all the topics related to CGM usage.

A special attention will be accorded to the specific topics related to AHCL algorithm functioning, with "Let the algorithm work" treatment attitude.

3. EVENT DEFINITIONS AND REPORTING REQUIREMENTS DURING THE STUDY

Definitions:

Adverse Event (AE) (ISO14155-2) Any untoward medical occurrence in a subject An AE can, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product or medical device, whether or not related to the medicinal (investigational) product or medical device.

Serious Adverse Event (SAE) (ISO 14155-2) An adverse event that (a) Led to a death (b) Led to a serious deterioration in the health of the subject that • resulted in life threatening illness or injury, • resulted in a permanent impairment of a body structure or a body function • required in-patient hospitalization* or prolongation of existing hospitalization • resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function (c) Led to fetal distress, fetal death or a congenital abnormality or birth defect *Inpatient Hospitalization is defined as: 24 hour acute admission to the hospital based on urgent medical need rather than elective admission. Note: A planned hospitalization for pre-existing condition, or a procedure required by the CIP, without a serious deterioration in health, is not considered to be a serious adverse event.

Serious Adverse Device Effect (SADE) (ISO 14155-2) Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Unanticipated Adverse Device Effect (UADE) (21 CFR 812.3(s)) Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

"Severe Hypoglycemia" is an event requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration. (American Diabetes Association Workgroup on Hypoglycemia, Diabetes Care 28:1245-1249, 2005)

"Severe Hyperglycemia" is defined as Hyperglycemia (blood glucose >270 mg/dL) with blood glucose ketones >0.6mmol/L or accompanied by symptoms of nausea, vomiting or abdominal pain.

"Diabetic Ketoacidosis/DKA" is defined as: Hyperglycemia (blood glucose >250 mg/dL or >13.9 mmol/L) with either low serum bicarbonate (<15 mEq/L) and/or low pH (<7.24) Anion gap (> 12) and either ketonemia or ketonuria and requiring treatment within a health-care facility. (American Diabetes Association-Diabetes Care, Volume 27, Supplement 1, January 2004).

The relatedness of the event to the study device or procedures will be determined for each adverse event.

The following definitions should be considered when determining the relationship of the event to the device or study procedure:

- Definite – clearly related to the device or procedure
- Probable – likely related to the device or procedure
- Possible – may be related to the device or procedure
- Unlikely – doubtfully related to the device or procedure
- Not Related – clearly not related to the device or procedure
- Unknown – not enough information exists to determine

Details of related adverse events, including episodes of severe hypoglycaemia, diabetic ketoacidosis, lipohypertrophy and injection/ infusion site infections, will be collected at each study visit and reported according to the requirements of the Bioethical Committee and to Medtronic. Adverse events will be captured by patients, carers and clinicians treating diabetes, and from interrogation of local hospital databases for details of hospital attendances.

4. AVOIDANCE OF BIAS

Participants will be randomised using a secure web-based randomisation programme. Participants will be randomised to each treatment arm in a 1:1 ratio. The randomisation code will be generated by a statistician using block randomisation with the random variable block size method.

Missing data will be monitored and strategies developed to minimise its occurrence; however, as much data as possible will be collected about the reasons for missing data and this will be used to inform the handling of missing data.

5. INFORMATION ABOUT QOL QUESTIONNAIRE

The following QOL questionnaire will be used: Speight J, Woodcock AJ, Reaney MD, Amiel SA, Johnson P, Parrott N, Rutter MK, Senior P, Smith R, Shaw JAM. The 'QoL-Q Diabetes' – a novel instrument to assess quality of life for adults with type 1 diabetes undergoing complex interventions including transplantation; presented at the Diabetes UK Professional Conference (Liverpool, UK: March 2010).

The questionnaire will be translated by study team under translation agreement along with Linguistic Validation Guidelines obtained from authors.

6. DATA HANDLING AND RECORD KEEPING

The investigator will retain all records and documents pertaining to this study. Data will be stored in a University Hospital in Krakow Data Archive Database. The Investigator will retain the source documents from which the information entered on the eCRF was derived. These records are to be retained in a secure storage facility maintained by the Investigational Center until 2 years after termination of the study. The Investigator should not dispose of these records without the approval of the Sponsor.

All data required for analysis will be captured on Case Report Forms (CRFs) developed by investigator. The Investigator will ensure that all CRFs are completed promptly, completely, and accurately. Information on case report forms will conform to the information in the source documents.

7. STATISTICS CONSIDERATIONS: SAMPLE SIZE CALCULATION AND STATISTICAL ANALYSIS

Statistical Hypothesis

The null-hypothesis H_o: $TIR_{MD/CSIII} = TIR_{AHCL}$ will be tested against the alternative hypothesis H_A: $TIR_{MDI/CSII} \neq TIR_{AHCL}$, where $TIR_{MDI/CSII}$ and TIR_{AHCL} are the mean Time in Range (70–180 mg/dL) in the MDI/CSII and the AHCL groups, respectively.

Sample size

Using data from the study previously performed at our center a mean TIR=80% (Std=15%) in the AHCL group and a mean TIR= 65% (Std=15%) in the MDI/CSII group. For a two sided two-sample t-test, a total sample size of 40 subjects is required to test the hypothesized difference in population means of 15% with a 95% confidence level, 80% power and attrition rate of 15%.

Analysis of primary endpoint

The primary analysis will use a two-sample t-test to compare the mean TIR between the randomized arms of the study. The analysis will be adjust by baseline TIR. The mean TIR in the patients in the AHCL arm will be claimed to be smaller than then mean TIR in the MDI arm if the average TIR is smaller in the AHCL arm and the associated p-value of the test is less than 0.05. No extra adjustments are needed for this nested test.

8. INFORMATION ABOUT MONITORING AND INSURANCE

All records and documents pertaining to this study will be available for inspection by the appropriate regulatory agencies.

All the study participants will be insured, the insurance costs are included into the budged proposal.

9. ETHICAL CONSIDERATIONS, REGULATORY APPROVAL PROCESS INFORMATION, REGISTRATION ON CLINICALTRIALS.GOV

The study protocol and consent form will be presented for approval to the local institutional ethics committee. The study will not be started until the written approval is granted. The study will be conducted in line with the Good Clinical Practice provisions of the Declaration of Helsinki with all

amendments and local regulatory requirements. Written Patient Informed Consent (PIC) will obtained from all participants before enrolment;

Individuals who will participate to the study will be informed that they will not be guaranteed the use of the pump either during or at the end of the study. However, those pump participants who express a preference to continue therapy and have measurable evidence of will be supported by their diabetes team in seeking the options l for continuation of pump therapy.

Participants will be free to withdraw their participation to the study at any time.

10. REPORTING OF ADVERSE EVENT

The Investigator will report to sponsor ALL adverse events that occur during the subject's participation in the clinical study. A pre-existing medical condition will only be documented as an adverse event if the condition worsens during the course of the subject's participation in the study. To provide further clarification, any adverse event that is determined to be related to the study (procedure and/or devices, anticipated or unanticipated) will be reported to sponsor along with those adverse events not related to device or study procedure. Non-serious Adverse events will be reported to the sponsor within 14 days of subject report to the site. For serious adverse events, reporting will be required to sponsor within 24 hours of site awareness.

A complete description of the event including treatment and interventions provided by medical professionals will be included on the AE CRF. The investigator will provide the sponsor with the necessary medical records to support the adverse event. Throughout the course of the study, Investigational Center staff will make all efforts to remain alert to possible reportable adverse events or untoward findings. Reports of adverse events will be requested from subjects at each visit and adverse event CRFs will be completed. Investigational Center staff will assess the intensity of each adverse event and its relationship to study procedures or devices.

Adverse events that will be assessed to have a relationship to a study procedure or study device will be analyzed by the Medtronic to determine whether or not there is a connection to mis-use of the device(s) or user error.

Events that are moderate and severe in intensity, all SAE, SADE and UADE that have not resolved at the time of the subject's discontinuation or completion of the study will be followed until the medical outcome is determined or until no further change in the condition is expected.

11. PRACTICAL VALUE AND FURTHER RESEARCH

We expect to see a significant improvement in both clinical outcomes and Quality of Life in patients who are naïve to pump and CGM technologies as they onboard on AHCL system. The consequence will be to broaden the population considered eligible to AHCL therapy and provide for the improvement of access.

12.PUBLICATION PLANS

We shall disseminate findings to study participants and through peer reviewed publications and conference presentations. The conferences of choice to present outcomes of our study will be:

- ATTD
- EASD
- ADA

Journals of choice where we will try to publish our study:

- Diabetes Care (first choice)
- Diabetologia (second choice)

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