Control-IQ Technology in Individuals with Type 2 Diabetes (2IQ)

Statistical Analysis Plan

Version 1.0

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Based on Protocol Version 3.0

Version History

Version	Author	Approvers	Effective Date	Study Stage	Protocol Version
1.0	Dan Raghinaru	Craig Kollman	11/17/2021	Protocol development and study approval	3.0

Approvals

Role	Digital Signature or Handwritten Signature/Date
Author and Statistician: Dan Raghinaru, JCHR	Dan Raghinaru I am digitally signing this document. 2021-11-17 11:02-05:00
Senior Statistician: Craig Kollman, JCHR	Craig Kollman I am digitally signing this document 2021-11-17 11:34-05:00
Coordinating Center Director: John Lum, JCHR	John Lum I am electronically signing this document 2021-11-17 14:16-05:00
Sponsor: Jordan Pinsker, Tandem Diabetes Care, Inc.	Jordan Pinsker Digitally signed by Jordan Pinsker Date: 2021.11.17 11:34:08 -08'00'

1. Study Overview

The following table gives an overview of the 2IQ study.

Table 1. Study Overview

PARTICIPANT AREA	DESCRIPTION
Title	Control-IQ Technology in Individuals with Type 2 Diabetes (2IQ)
Précis	A prospective, single-arm study of 6 weeks of home use of the Control-IQ automated insulin delivery system in individuals with type 2 diabetes age 18 and older.
Investigational Device	t:slim X2 insulin pump with Control-IQ technology v1.5 (Control-IQ System)
Objectives	The objectives of the study are to assess safety and explore glycemic outcomes with use of a closed loop control (CLC) system (t:slim X2 with Control-IQ Technology) in adults with type 2 diabetes to provide data to design a subsequent larger study.
Study Design	After an initial run-in period to ensure that participants can successfully use the study CGM and study pump in open-loop mode, all participants will use the study system (pump and CGM) in closed-loop mode for 6 weeks.
Number of Sites	~3 US clinical centers
Key Safety Endpoints	Key Safety Endpoints: • Severe Hypoglycemia • Diabetic Ketoacidosis and Hyperosmolar Hyperglycemic Syndrome • Other reportable adverse events • Unanticipated adverse device effects
Other Endpoints	Other Endpoints: • CGM-measured % below 54 mg/dl • CGM-measured % above 180 mg/dL • CGM-measured post-prandial glycemic peak • Various other CGM-measured glycemic outcomes over 24 hours, daytime, and nighttime, as well as CGM outcomes with respect to announced meals • Total daily insulin use, daily basal and bolus insulin, and Weight *Primary and secondary endpoints will be analyzed in total together, as well as separately for Group A (prior users of basal insulin only) and Group B (prior users of multiple daily injections) participants.*
Population	**Inclusion Criteria** 1. Age ≥18 years old and residing in the US 2. Clinical diagnosis, based on investigator assessment, of type 2 diabetes for at least one year 3. Using a stable insulin dose for at least 3 months, to include A) basal insulin only, or B) MDI, to include CSII (including use of AID systems other than Tandem Control-IQ) 4. Total daily insulin dose ≤200 units/day

PARTICIPANT AREA	DESCRIPTION
	5. Willing to use only aspart (novolog) or lispro (humalog) insulin with the study pump, with no use of concentrated insulin above U-100, long-acting basal insulin injections, or inhaled insulin 6. For females, not currently known to be pregnant *If female of child-bearing potential, must agree to use a form of contraception to prevent pregnancy while a participant in the study as documented in the study records. A negative serum or urine pregnancy test will be required for all females of child-bearing potential. Participants who become pregnant will be discontinued from the study. Also, participants who during the study develop and express the intention to become pregnant within the timespan of the study will be discontinued.* 7. HbA1c $\geq$ 7.5% and $\leq$ 12% at screening 8. Has current glucagon product to treat severe hypoglycemia (injectable or nasal) at home (*will provide prescription if they do not have one*) 9. Be willing to exercise for 30 minutes or more at least once per week during the main phase of the study 10. Has the ability to read and understand written English. 11. Investigator believes that the participant has the capacity such that they can provide informed consent and successfully and safely operate all study devices and is capable of adhering to the protocol and completing the study **Exclusion Criteria** 1. Prior use of Tandem t:slim X2 insulin pump with Control-IQ technology 2. Two or more episodes of severe hypoglycemia (needing assistance) in the past 6 months 3. History of inpatient psychiatric treatment in the past 6 months 4. History of drug abuse (defined as any illicit drug use) or history of alcohol abuse prior to screening or unwillingness to agree to abstain from illicit drugs throughout the study. 5. History of significant heart disease, lung disease, liver disease, chronic kidney disease, or other systemic disease determined by investigator to interfere with the study, or make required exercise unsafe 6. History of significant vision, hearing, or dexterity problems that will impair use of the closed loop system 7. Use of glucocorticoids, beta blockers, sulfonylureas, meglitinides or other medications specifically listed in section 8.3 of the protocol or determined by investigator to interfere with the study 8. Unstable dose of SGLT-2 inhibitor, GLP-1 receptor agonist, or other adjuvant medication specifically listed in section 8.3 of the protocol, or starting a new glucose lowering agent during the trial. 9. Unstable dose of any medication used for weight loss, as listed in section 8.3 of the protocol, or starting a new medication for weight loss during the trial. 10. Abnormal screening electrocardiogram consistent with increased risk during exercise, such as arrhythmia, ischemia, or prolonged QTc interval (>450 ms) 11. History of hemodialysis 12. History of adrenal insufficiency 13. Uncontrolled hypo- or hyperthyroidism

PARTICIPANT AREA	DESCRIPTION
	14. Significant diabetes related complications, based on investigator assessment 15. Immediate family member (spouse, biological or legal guardian, child, sibling, parent) who is an investigative site personnel directly affiliated with this study or who is an employee of Tandem Diabetes Care, Inc.
Sample Size	Up to 30 individuals initiating use of the study system in closed-loop mode, with the goal of at least 24 completing the trial
Treatment Groups	All participants will use the study-assigned Control-IQ pump in closed-loop mode.
Participant Duration	~8-12 weeks, depending on duration of run-in phase
Study Duration (planned)	~5 months from first enrollment until last participant visit
Protocol Overview/Synopsis	After consent is signed, eligibility will be assessed. Eligible participants not currently using a Dexcom G6 CGM or using a Dexcom G6 CGM with <85% of possible glucose values captured during the 14 days prior to enrollment will initiate a CGM run-in phase of 2-4 weeks. Participants who skip or successfully complete the CGM run-in will be trained on use of the study pump in open-loop mode and will initiate a pump run-in phase of 2-4 weeks that will include insulin therapy adjustment to optimize open-loop glycemic control. Participants who successfully complete the open-loop pump run-in will be trained on use of the study pump in closed-loop mode and will use the study system (pump and CGM) in closed-loop mode for 6 weeks. Subjects will be asked to use programmed sleep activity each night and perform exercise challenges with exercise mode enabled at least once per week. Questionnaires will be given at the screening visit after consent; before starting closed-loop use (Control-IQ Phase); and after 6 weeks of closed-loop use. Semi-structured interviews will be performed at the end of the study to better determine the experience of using the study device <u>Study Safety Plan</u>: Participants will be given a blood glucose and ketone meter to use throughout the study, and will be trained on their use by qualified staff. BGM readings will be performed in accordance with the study safety plan and per CGM manufacturer instructions. Ketone readings will be performed per the study safety plan. Site investigators may adjust insulin delivery profile settings as needed throughout the study in accordance with their clinical practice.

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The following table provides an overview of the schedule of study visits, phone contacts, and key procedures.

Table 2: Schedule of Visits and Procedures

	Screen-ing Visit	CGM Run-in Visit (may be repeated after 2 weeks)	Pump Training Visit and Settings Optimization (may be repeated after 2 weeks)	Control-IQ Closed-Loop Training Visit	Control-IQ Closed-Loop Use							
		2-4 weeks	2-4 weeks		3d	1w	2w	4w	6w	+3d	UV	Exercise[3]
Visit (V) or Contact (C)	V	V	V	V	C	C	V	C	V	C	V/C	C
Informed Consent	X											
Eligibility Assessment	X											
Medical history/ physical exam	X											
Height, weight, blood pressure and pulse	X			X[2]					X[2]			
HbAlc (POC or local lab)	X											
Central Lab: C-peptide and Glucose; HbA1c	X											
ECG	X											
Pregnancy test (females of child-bearing potential)	X			X								
Questionnaires/Surveys	X		X	X					X			
Semi-structured interview									X[1]			
Assessment of CGM use	X	X										
Study system training		X	X	X							X	
AE Assessment		X	X	X	X	X	X	X	X	X	X	X
Upload device data from home					X	X		X			X	
Download device data at clinic visit		X	X	X			X		X		X	

[1] Interview completed within 28 days of completion of 6-Week visit

[2] Weight only

[3] Participants will be instructed to contact study staff after each exercise challenge to review AE's and diabetes management around exercise.

2. Statistical Hypotheses

The primary outcomes for this study are CGM-measured percentage below 54 mg/dl and CGM-measured percent above 180 mg/dl over a 6-week period. The intervention will be considered effective if the 6-week follow-up % above 180 mg/dl value is superior and % below 54 mg/dl value is non-inferior to the corresponding baseline values using a statistical significance of α=0.05 and the analysis specified below in Section 7 (i.e., $p < 0.05$).

The null/alternative hypotheses are:

Percentage below 54 mg/dl (non-inferiority):

1. *Null Hypothesis*: The difference in mean CGM-measured % below 54 mg/dl between the 6 weeks follow-up and baseline is greater than or equal to +1%.
2. *Alternative Hypothesis*: The difference in mean CGM-measured % below 54 mg/dl between the 6 weeks follow-up and baseline is less than +1%.

Percentage above 180 mg/dl (superiority):

1. *Null Hypothesis:* There is no difference in mean CGM-measured % above 180 mg/dL between the 6 weeks of follow-up and baseline.
2. *Alternative Hypothesis*: The mean CGM-measured % above 180 mg/dL is different at baseline than the mean over 6 weeks of follow-up.

3. Sample Size

The planned cohort of N=30 participants, with the goal of at least N=24 completing the study, is a convenience sample not based on statistical principles.

4. Outcome Measures

4.1. Primary Efficacy Endpoint:

- Non-inferiority in CGM-measured % below 54 mg/dl between the 6 weeks follow-up. This is the only non-inferiority and one-sided outcome in the study.
- Superiority in CGM-measured % above 180 mg/dl between the 6 weeks follow-up.

4.2. Secondary Efficacy Endpoints

- CGM overall metrics during follow-up:
  - % in range 70-180 mg/dL
  - % in tight glycemic range 70-140 mg/dL
  - mean glucose
  - glucose variability measured with the coefficient of variation
  - % <70 mg/dL
  - % <54 mg/dL (superiority)

- % >250 mg/dL
- % >300 mg/dL

- CGM metrics by time of day:
  - Calculate all CGM metrics listed above (including the two primary outcomes) for:
    - All 24 hours of the day (the two primary outcomes are over 24hr)
    - Daytime only (06:00AM to 00:00AM)
    - Nighttime only (00:00AM to 06:00AM)
    - During and after the scheduled exercise sessions
- Up to 4hr post-prandial CGM metrics:
  - Area Under the Curve (AUC)
  - Maximum
- Insulin over follow-up:
  - Total daily insulin (units and units/kg)
  - Total daily bolus (units and units/kg)
  - Total daily basal (units and units/kg)
- Weight and body mass index at 6 weeks
- Questionnaires:
  - Administered at enrollment only
    - Tandem Study-Specific Survey – 4 items.
    - Altarum Consumer Engagement Measure – 6 items and total score.
  - Administered at the start of open-loop and again at the start of the closed loop
    - Tandem Pump Training Survey – 4 items.
  - Administered at enrollment, start of closed-loop period, and 6 weeks
    - DAWN Impact of Diabetes Profile – 7 items and total score.
    - Diabetes Impact and Device Satisfaction Scale – 12 items and two subscale scores (device satisfaction and diabetes impact).
    - PROMIS Sleep-Related Impairment Questionnaire – 8 items and total score.
  - Administered at the start of closed-loop period and at 6 weeks
    - System Usability Scale – 10 items and total score.

4.3 Calculation of Overall CGM Metrics (primary and secondary):

- <u>One Week of Baseline:</u> The last 7 days of personal CGM data before enrollment or last 7 days of CGM run-in data will serve as baseline. If a participant has <24hr of data in the last 7 days of CGM personal or run-in and if more CGM data are available beyond the 7 days, then will go backwards 24hr at one time until the minimum of 24hr of CGM data are reached. At least 24hr of data during baseline are required for the glycemic metrics to be calculated. These are Dexcom sensor data.
- <u>Six Weeks of CLC use</u>: All CGM data following the midnight of the initiation of CLC use visit day and the midnight right before the end of study visit day will be included irrespective if the system was in closed-loop mode or not. Since the exercise sessions are designed as challenges to the system and the data to be analyzed for safety events, the CGM data between the start of the exercise and 6:00AM next morning will be analyzed separately (see Section 8.1 below) and not included here. On the other hand, since the meals are not designed to be challenges to the system, the CGM data following the meals will be included here even if also analyzed separately (see

Section 8.1 below). If the end of 6 weeks of CLC use visit is more than 6 weeks away from the CLC use initiation visit for a participant, then the CGM data will be truncated at 6 weeks (i.e., 42 days). At least 168hr of data during these 6 weeks of CLC use are required for the glycemic metrics to be calculated and for a participant to be included in the primary and secondary analyses. These are Tandem pump CGM data and will include data following meals and during exercise periods.

- Two-four Weeks of Open Loop (OL) use: All CGM data between the initiation of Open-Loop use and the start of CLC will be used. At least 24hr of data during this period are required for the glycemic metrics to be calculated. These are Tandem pump CGM data.
- All CGM metrics during baseline, OL, and CLC periods will be calculated giving equal weight to each sensor reading for each participant.

4.4 Calculation of Post-Prandial CGM Metrics

- This analysis will be limited to participants using meal boluses.
- Meal boluses will be identified by a carb announcement >15g in the pump log.
- Will be calculated only during the 6 weeks of CLC use and are based on the Tandem pump CGM data.
- In case a participant switches between basal-only and basal plus boluses; only meals during bolus use can be identified and included in these analyses.
- Will include all CGM data between the carb announcement and the earlier of 4hr from the end of the meal or the beginning of the next meal bolus or exercise session.
- At least 30min (or 6 CGM readings) are required for each individual meal for the CGM metrics to be calculated.
- Each CGM reading following a particular meal will be given equal weight.
- The unit of analysis is an individual meal and any participant with at least one meal will be included in these analyses.

4.5 Calculation of CGM Metrics during Scheduled Exercise Sessions and the Following Night

- Will be calculated only during the 6 weeks of CLC use and are based on the Tandem pump CGM data.
- Will be calculated only if the exercise session was recorded on CRF.
- All data between the start of the exercise challenge and 6:00AM next morning will be included.
- For each exercise, two different periods will be considered, and two separate glycemic metrics will be calculated:
  - During and two hours following the end of the exercise – the period between the start and 2 hours following the end of exercise as recorded on CRF, and
  - Overnight following the exercise – the period between 2 hours following the end of the exercise and 6:00AM next morning.
- At least 30min (or 6 CGM readings) are required for each one of the two periods associated with an individual exercise session for the CGM metrics to be calculated.
- Each CGM reading during an exercise session will be given equal weight.
- The unit of analysis is an individual exercise session and any participant with at least one exercise challenge completed will be included in these analyses.

4.6 Calculation of Insulin Metrics

- Will include only days with complete insulin data and at least 7 such days are required for the metrics to be calculated. If there are not such 7 days, the participants will not be included in the insulin analyses. Since Tandem pump automatically generates a basal record every hour, at least 20 such hourly records are required for a day to be considered complete with insulin data and to be counted towards the minimum of 7 days.
- Will be calculated only during the 6 weeks of CLC use and are based on the Tandem pump insulin delivery data.
- As with the CGM metrics, if a participant stayed in the study more than 6 weeks, then the insulin data will be truncated at 6 weeks from the initiation of CLC use.
- Weight at baseline will be used to calculate units/kg metrics.

4.7. Questionnaires

Participants are allowed to skip specific questionnaires or items within a questionnaire. The data might therefore include some missing items. If applicable, questionnaires will be scored according to the instructions given in the manual. If a total or a sub-scale score is calculated but no instructions exist, then at least 75% of the items should be non-missing for the total or sub-scale score to be calculated.

4.8 Analysis Windows

Analysis windows apply to the following outcomes measured at 6-week final visit:

- Weight
- Questionnaires

To be included in the corresponding analyses, these data must be collected between days 28 and 56 from the beginning of CLC period. The target date is 42 days from the beginning of CLC period.

This does not apply to the CGM and insulin metrics which are calculated as described above.

5. Description of Statistical Methods

5.1. General Approach:

- Since this is not a randomized trial, the intention-to-treat (ITT) principle does not apply.
- In the unlikely event that an enrolled participant is later found to be ineligible, the participant will be excluded from all analyses.
- Otherwise, all enrolled participants with at least 168h of CGM data during the 6-week of CLC use will be included in the primary and secondary analyses.
- The primary and secondary CGM analyses will include the baseline and the 6-week of CLC use periods. All p-values that will be calculated refer to these paired baseline-CLC differences.
- All p-values, apart from the primary CGM-measured % below 54 mg/dL, will be two-sided.
- Only CGM metrics, weight/BMI, and some questionnaires are measured both at baseline and follow-up. As such, p-values will be calculated only for CGM and weight/BMI metrics.
- Standard diagnostics, based on the paired differences between the CLC and baseline periods, will be performed for all analyses. If the paired differences do not follow an approximate normal

distribution, then a non-parametric comparison based on ranks will be performed. Previous experience suggests that no nonparametric analyses will be necessary for % time in range 70-180 mg/dL, % above 180 mg/dL, or mean glucose. Other outcomes like % below 54 mg/dL are skewed; however, the differences between the two periods may follow a normal distribution and there may be no need for nonparametric analyses.

- Exploratory CGM analyses will include all three periods: baseline, OL, and CLC use. No p-values will be calculated for these exploratory analyses; but only summary statistics like mean (SD) or median (IQR) and plots.

5.2 Analysis Cohorts

Primary and Secondary Analyses:

- All participants with at least 168hr of CGM data during the CLC use period will be included in the CGM-based analyses.
- All participants with at least one post-prandial or with one scheduled exercise and with CGM data during these periods will be included in the corresponding analysis.

Per Protocol (PP) Analyses:

- A per-protocol analysis for the two primary outcomes will be limited to participants who used the CLC for at least 80% of the time during the 6-week period. If fewer than 10% of the study participants would be excluded based on this criterion, then the per-protocol analysis will not be performed.

Safety Analyses:

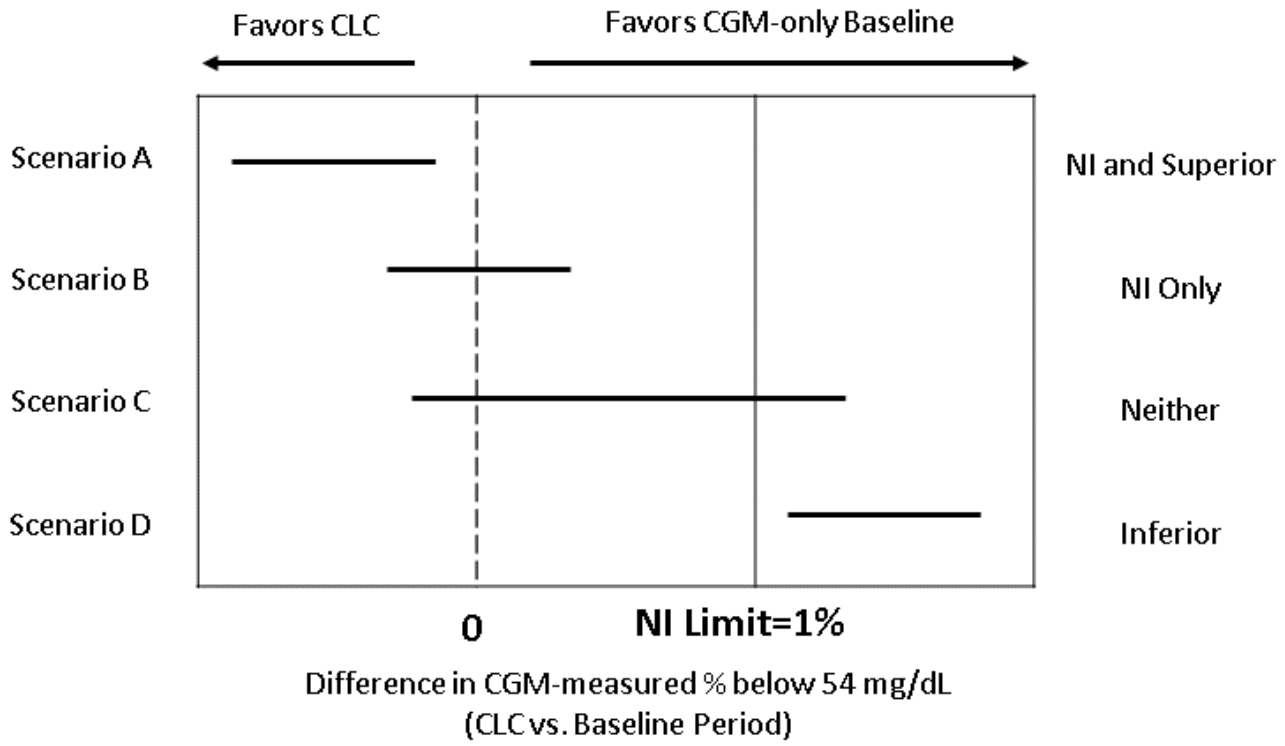
- Safety analyses will include all participants and all the data until the end of the study. Safety outcomes will be reported by each one of the three periods: run-in, OL, and CLC use.

6. Primary Analyses

The primary outcomes are non-inferiority in % time below 54 mg/dl and superiority in % time above 180 mg/dl during the 6-week of CLC use when compared with one week of baseline CGM-only use. Summary statistics (mean ± SD or median (quartiles)), scatterplots, and boxplots and will be reported for the two CGM-measured outcomes at baseline, during 6-weeks of CLC use, and the difference between the two periods.

A paired t-test will be used. Primary analyses will report the point estimate, 95% confidence interval, and p-value for the paired differences. If the paired differences are highly skewed, then a non-parametric rank-test, equivalent with a paired t-test, will be used instead. It is expected that the paired differences for both primary outcomes will follow a normal distribution, even if the % time below 54 mg/dl values will not.

CGM-measured % below 54 mg/dL will be a non-inferiority test with limit +1%. Since non-inferiority is typically framed in terms of a one-sided test, it is worth noting that the left half of a two-sided test at alpha = 0.05 gives the same rejection region as a one-sided test at alpha = 0.025. Therefore, reporting a two-sided 95% confidence interval will provide flexibility to also test for inferiority if non-inferiority cannot be declared, or superiority if non-inferiority is declared. The following figure shows examples of the inference to be drawn for a non-inferiority analysis based on the two-sided 95% confidence interval in various scenarios:



7. Analysis of the Secondary Endpoints

7.1 Secondary CGM Metrics

The analyses for the continuous and overall CGM-measured outcomes will parallel those mentioned above for the primary outcome.

There will be no comparisons or formal testing for the analyses of post-prandial and exercise challenge glycemic outcomes. Both will be descriptive analyses and will include summary statistics (mean ± SD or median (quartiles)), scatterplots, boxplots, and/or individual meals or exercise CGM and insulin tracings. Meals may be grouped by type (breakfast, lunch, dinner), amount of carbohydrates, and announcement in the pump or not. Exercises analyses will be grouped by the two periods (during plus up to 2hr after the end of exercise and nighttime following the exercise) and may also be grouped by length, intensity, or type of exercise.

7.2. Insulin Analyses

Summary statistics appropriate to the distribution for total daily basal, bolus, and insulin and boxplots will be generated.

7.3. Weight and Body Mass Index Analyses

Summary statistics appropriate to the distribution for weight and BMI will be given at enrollment and the end of study. A paired t-test or equivalent non-parametric test will be calculated as mentioned above for the primary outcomes.

7.4. Questionnaires

For each questionnaire, summary statistics (mean ± SD and n(%)) will be given for each item and at each time point when the questionnaire was administered. For questionnaires with a scoring guide available that are administered at both the start of closed loop and again at 6 weeks – that is for DAWN Impact, Diabetes Impact, PROMISE Sleep, and System Usability total or subscale scores - a paired t-test or equivalent non-parametric test will be calculated as mentioned above for the primary outcomes.

8. Safety Analyses

All enrolled participants will be included in these analyses and all their safety events up to the final visit will be reported.

The circumstances of all reportable cases of the following will be summarized and tabulated by study period (run-in, OL, CLC):

- Severe hypoglycemia (needing assistance)
- DKA
- Hyperosmolar Hyperglycemic Syndrome
- Serious Adverse Events
- Unanticipated adverse device effects
- Ketone events defined as a calendar day with ketone level >1.0 mmol/L

Additionally, the number of events and the event rate per 100 person-years during CLC use will be calculated for each of the safety outcomes listed above.

9. Device Issues

The following tabulations and analyses will be performed to assess device issues:

- Device malfunctions requiring study team contact and other reported device issues.
- Rate of different failure events and alarms per 24 hours recorded by the Control-IQ system – overall and by study week.

10. Protocol Adherence and Retention

The following measures of adherence will be tabulated during the 2-4 weeks of OL and during the 6 weeks CLC follow-up periods:

- Number of protocol and procedural deviations
- Flow chart accounting for all enrolled participants up to end of study
- Flow chart of all enrolled participants at all scheduled visits and phone contacts post treatment initiation
- Number of and reasons for unscheduled visits and phone calls
- Number of participants who stopped OL or CLC use and reasons

11. Intervention Adherence

Descriptive summary statistics will be given for the percentage of time that the CLC is in active mode and the amount of CGM use over the 6-week CLC use period. A scatterplot of these two percentages will be constructed.

Boxplots will be given for each of these percentages for each one of the 6 weeks of follow-up.

Descriptive statistics will be given for the percentage of time spent in each of the CLC operational modes.

12. Baseline Descriptive Statistics

Baseline demographic and clinical characteristics of the cohort of all enrolled participants will be summarized in a table using summary statistics appropriate to the distribution of each variable. Descriptive statistics will be reported for the following:

- Age
- Sex
- Race/Ethnicity
- Diabetes duration
- Insulin method before enrollment (basal only or multiple daily injections)
- CGM use before enrollment
- HbA1c
- BMI
- Participant-reported number of SH and DKA 12 months prior to the start of the study
- Baseline and OL CGM metrics including:
    - % time < 54 mg/dl
    - % time > 180 mg/dl
    - % in range 70-180 mg/dl
    - mean glucose
    - % time < 70 mg/dl

13. Planned Interim Analyses

No formal interim efficacy analyses are planned for this study.

The medical monitor will review all cases of severe hypoglycemia and diabetic ketoacidosis irrespective of device relationship, all device related SAEs, and all UADEs at the time that they occur during the study and will review compiled safety data at periodic intervals. The medical monitor or sponsor can request modifications to the study protocol or suspension or outright stoppage of the study if deemed necessary.

The data to be reviewed periodically by the medical monitor and sponsor will include information regarding the following:

- Status of enrolled participants
- Recruitment rates by month and by site
- Baseline demographic and clinical characteristics
- Dropped participants and reasons for discontinuing
- Protocol deviations
- Device issues
- Scheduled and unscheduled visits and contacts
- Frequency of CGM and system use
- Reportable adverse events as described above
- CGM-based hypo- and hyper-glycemic events during baseline, OL, and CLC periods

14. Subgroup Analyses

In exploratory analyses, each one of the two primary outcomes (% time <54 mg/dl and % time >180 mg/dl) will be tested separately for baseline factor interaction with the changes in outcome from baseline to CLC period. Summaries appropriate to the distribution will be reported and a least squares regression will be fit with the dependent variable being the paired difference (value during CLC use minus value at baseline) and the subgroup factor as an independent variable. HbA1c will be analyzed as a continuous independent variable.

Interpretation of subgroup analyses will be viewed with caution, particularly in the absence of an overall significant difference. Subgroups will be analyzed according to the following baseline factors:

- Gender
- Race/Ethnicity (if enough numbers in more than one category)
- HbA1c (approximate median will be used to create two display categories)

- Insulin
  - Basal only (Group A)
  - Multiple daily injections (Group B)

15. Multiple Comparison/Multiplicity

There will be no formal correction for multiple comparisons in this pilot study.

16. Exploratory analyses

No p-values will be calculated for these analyses.

The primary analyses described above will be repeated with the CGM-measured % below 54 mg/dl and % above 180 mg/dl during follow-up limited to times when the CLC was in active mode.

Weekly boxplots for selected glycemic and insulin metrics will be generated.

The overall glycemic and the insulin analyses will be extended to include the 2-4 weeks OL period.