Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: The RealTrend study

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**Objective:** To compare the improvements in glycemic control associated with transitioning to insulin pump therapy in patients using continuous glucose monitoring versus standard blood glucose self-monitoring.

**Research design and methods:** The RealTrend study was a 6-month, randomized, parallel-group, two-arm, open-label study of 132 adults and children with uncontrolled type 1 diabetes (HbA1c ≥ 8%) being treated with multiple daily injections (MDI). One group was fitted with the Medtronic Minimed Paradigm REAL-Time system (PRT group), an insulin pump with integrated continuous subcutaneous glucose monitoring (CGM) capability, with instructions to wear CGM sensors at least 70% of the time. Conventional insulin pump therapy was initiated in the other group (CSII group). Outcome measures included HbA1c and glycemic variability.

**Results:** A total of 115 patients completed the study. Between baseline and trial end, HbA1c improved significantly in both groups (PRT group, -0.81 ± 1.09%, \( P < 0.001 \); CSII group -0.57 ± 0.94%, \( P < 0.001 \)), with no significant difference between groups. When considering the 91 patients who were fully protocol-compliant (including CGM sensor wear ≥ 70% of the time), HbA1c improvement was significantly greater in the PRT group (\( P = 0.004 \)) (PRT group -0.96 ± 0.93%, \( P < 0.001 \); CSII group -0.55 ± 0.93%, \( P < 0.001 \)). Hyperglycemia parameters decreased in line with improvements in HbA1c with no impact on hypoglycemia.

**Conclusions:** CGM-enabled insulin pump therapy improves glycemia more than conventional pump therapy during the first 6 months of pump use in patients who wear CGM sensors at least 70% of the time.
The long-term clinical benefit of tight glycemic control in type 1 diabetes (T1DM) patients has been demonstrated in several reports by the Diabetes Control and Complications Trial (DCCT) (1,2). To achieve this goal, insulin analogs, basal-bolus Multiple Daily Injections (MDI) and insulin pumps for Continuous Subcutaneous Insulin Infusion (CSII) have proved important tools for lowering glucose variability and improving glycemic control, leading to higher treatment satisfaction in patients with T1DM (3-5).

Nevertheless, intensive treatment of T1DM often does not succeed in achieving target HbA1c levels ≤ 7.0% (6). Increased self-monitoring of blood glucose levels (SMBG) is correlated with better HbA1c levels (7, 8), but for practical reasons most patients do not perform more than 5-7 SMBG per day. Consequently, postprandial hyperglycemia and nocturnal hypoglycemia often remain unnoticed even in well-controlled individuals (9-11). Hence, detecting and treating these events might improve the patient’s glycemic control and impact quality of life.

Continuous Glucose Monitoring (CGM) provides information from a subcutaneous glucose sensor on interstitial glucose levels. A typical CGM system incorporates alarms for high and low glucose levels, and displays glucose trend information graphically allowing patients to anticipate hypo- and hyperglycemic events. Recent studies have shown that wearing such devices is associated with improved glycemic control in patients undergoing intensive therapy for T1DM (12,13) and in patients treated by CSII (14); however no study has investigated the benefit of CGM in patients with poor metabolic control on MDI upon initiation of pump therapy. In this trial we randomly initiated pump therapy in patients with insufficient metabolic control despite optimized basal-bolus injection regimens with either the Paradigm REAL-Time insulin pump (PRT, an insulin pump that can receive and display CGM data from a separate subcutaneous glucose sensor) or conventional CSII, and compared glycemic outcomes after 6 months.

RESEARCH DESIGN AND METHODS

132 patients (51 children, 81 adults) with T1DM were recruited in 8 centers (6 adult and 2 pediatric centers). Inclusion criteria required age between 2 and 65 years, T1DM diagnosed for ≥ 12 months, follow up by the respective investigator for at least 3 months, HbA1c ≥ 8% and treatment with basal/bolus MDI with rapid insulin analogs at mealtimes. Unbiased biochemical hyper- and hypoglycemia parameters were collected using a blinded Holter-type CGM at the beginning and the end of the trial. Patients randomized into the PRT group agreed to wear an unblinded glucose sensor during at least 70% of the study period. All patients continued to perform fingerstick measurements for glucose self monitoring as prior to the study.

The trial was registered on clinicaltrials.gov (number NCT00441129) and approved by the Ethical Committee: CPP Sud Méditerranée II. All patients (or the parents of minor patients) read the patient information and signed informed consent forms.

Study Treatment. Physicians and patients were blinded to centralized HbA1c data from baseline to completion of the study. HbA1c levels were measured at screening, baseline, 3, and 6 months.

Two weeks after screening (Visit 1), eligible patients were randomized to one of the two groups (PRT or CSII), and fitted with a Holter-type CGM for 3 days. Blinded CGM data were retrieved at the end of this period (Visit 2). Patients in the PRT group were
asked to start using only the (unblinded) CGM function of their insulin pump at this time and were free to use the CGM information provided to them as they desired, while continuing MDI treatment for 9 days. Default settings for the high and low glucose alarms could be adjusted by the physician for individual patients.

At Baseline (Visit 3, 12 days post-randomization), insulin pump therapy was initiated in both groups. Patients in the PRT group started using the pump function of their device, while patients in the CSII group were fitted with a Medtronic Minimed Paradigm 512/712 insulin pump. All patients continued to use their usual blood glucose meter to obtain at least 3 readings daily. Patients in the PRT group were required to use glucose sensors at least 70% of the time, replace the sensor every 3 days, and were instructed on appropriate responses to CGM information. A confirmatory blood glucose reading served as reference for therapeutic decisions.

One month after pump therapy initiation (Visit 4), device data were downloaded for both groups, and patients discussed treatment with the physician. Therapy could be adjusted for all patients and alarm targets reset for the PRT group.

After 3 months of pump therapy (Visit 5), pump and CGM data were downloaded again, blood samples were taken for HbA1c determination, and treatment guidelines were adjusted as needed.

Three days prior to the final study visit after 6 months of pump therapy (Visit 6), all patients again wore a blinded Holter-type CGM device. Blinded CGM, PRT and CSII data were downloaded at study end.

The primary objective of the trial was to determine whether pump therapy initiation in patients with HbA1c values $\geq 8\%$, being currently treated with MDI, could result in improved metabolic control after 24 weeks of continuous use of either a sensor-augmented or a conventional insulin pump. The secondary objective was to evaluate change in glycemic variability. The primary outcome was HbA1c change from baseline (Visit 3) to 6 months (Visit 6). Secondary outcomes included mean glucose change and descriptive parameters for biochemical hyperglycemia (>190 mg/dl) and hypoglycemia (<70 mg/dl). Daily insulin use was also compared.

The sample size calculation was based on change in HbA1c levels between baseline and trial end. A difference of 0.5% or more between the treatment groups was considered clinically meaningful. To have a 95% chance of detecting a 0.5% difference with an assumed standard deviation of 0.9, using a two-sided two-sample t-test with a power of 80%, 52 patients were required for each group. A total of 132 patients were randomized to allow for a normal dropout rate. Due to the nature of the treatments the study was not blinded.

**Statistical analysis.** The primary covariance analysis was based on the comparison of HbA1c changes between the PRT and CSII groups using the Last Observation Carried Forward (LOCF) method on the full analysis set (FAS) of patients (all patients with 2 HbA1c results from baseline to the end of the study). A $P$ value $\leq 0.05$ was considered statistically significant. Analyses were adjusted for age as patients were randomized within the age groups: $< 19$ years and $\geq 19$ years. In light of sensor use heterogeneity in the PRT group, a separate analysis was conducted using data from only those subjects who adhered to the protocol requirements (the per-protocol data subset).

Secondary outcomes analyzed the changes in glucose concentration (hyperglycemia and hypoglycemia above and below target range) calculated from blinded CGM data using the covariance analysis model. Daily use of insulin calculated from
pump downloads was compared between groups using an analysis of variance adjusted for age groups.

RESULTS

Patients. Between May 2006 and December 2007, 148 patients were assessed for eligibility and 132 (81 adults, 51 children) fulfilling the inclusion criteria were randomized. The safety population (n = 128) was identical to the randomized population except for 4 adults who withdrew before visit 3. The full analysis (FAS) population (n = 115) excluded an additional 13 patients who did not have HbA1c measured after the baseline visit. The FAS population included 55 patients in the PRT arm (22 children, 33 adults) and the 60 patients in the CSII arm (24 children, 36 adults). Analysis on this population was intention-to-treat. The per protocol (PP) population excluded 24 FAS patients because of major protocol deviations (1 screening failure in the CSII group and 23 patients in the PRT group who failed to wear glucose sensors at least 70% of the time). The PP population included 32 patients in the PRT group (11 children, 21 adults) and 59 patients in the CSII group (24 children, 35 adults).

A total of 20 patients abandoned the study: 14 from the PRT group (6 children and 8 adults) and 6 from the CSII group (6 adults). The trial ran from May 2006 to May 2008, with the first patients recruited in June 2006.

Patient characteristics at baseline were comparable in both study arms for all analyzable populations (Table 1).

HbA1c levels. In the FAS population, HbA1c levels were significantly reduced in both groups (PRT -0.81 ± 1.09%, P < 0.001; CSII -0.57 ± 0.94%, P < 0.001) but the difference in favor of the PRT group failed to reach statistical significance (p = 0.087) (Figure 1a). Among patients who were fully compliant with the protocol, however, the reduction in HbA1c was significantly greater in the PRT group (PRT -0.96 ± 0.93%, P < 0.001; CSII -0.55 ± 0.93%, P < 0.001; intergroup comparison: P = 0.004) (Figure 1b).

Glycemic control (Table 2). In the FAS population, the mean glucose concentration decreased in both groups between baseline and study end. The reduction was significantly greater in the PRT group (-1.7±3.0%) than the CSII group (-0.6±2.2%), p=0.005. Significant differences in favor of the PRT group were also observed with respect to duration of hyperglycemic events, in the hyperglycemic AUC/day, in the mean amplitude of glycemic excursions (MAGE) (15) and in overall standard deviation (SD) of blood glucose values. Similar trends of improved glycemic variability were observed in the PP population, although some failed to reach statistical significance due to the small sample size. All hypoglycemia parameters remained constant and comparable in both groups.

Insulin doses and use. In the FAS population, there was a significant increase in total daily doses (TDDs) of insulin between baseline and after one month of treatment in both the PRT group (ΔTDD=5.8±12.8U) and the CSII group (ΔTDD=2.2±8.4U; P = 0.032). Likewise, doses increased significantly between baseline and study end (PRT: 6.8±17.3U; CSII: 1.5±9.1U; p=0.036). Patients in the PRT group bolused more frequently after one month of treatment (PRT: 4.8±1.5; CSII: 4.1±1.2; p=0.002) and at study end (PRT: 4.7±1.4; CSII: 3.9±1.4; p=0.005). A higher percentage of insulin delivered as bolus (53.8±10.0%) in the PRT group vs CSII (49.8±15.8%) reflects these behavioral changes.

In the PP population, TDDs increased between baseline and 1 month (by 6.1±9.5 U in the PRT group and by 1.7±7.6U in the CSII group; p=0.028), but the difference failed to reach significance at 3 and 6 months while of comparable magnitude. PRT patients bolused
more frequently at 3 months (PRT: 4.8±1.2; CSII: 4.1±1.2; p=0.002) and at study end (PRT: 4.9±1.4; CSII: 3.9±1.4; p= 0.002). Bolus delivery accounted for 53.3±9.3% of total insulin in the PRT group vs. 49.7±15.9% in the CSII group.

**Ancillary analyses.** Between the screening visit and the end of the study, HbA1c levels fell significantly in both groups of the FAS population (PRT, -1.14 ± 1.21%, P < 0.001; CSII, 0.57 ± 0.91%, P < 0.001), and the difference in favor of the PRT group compared to the CSII group was statistically significant (P = 0.006). HbA1c levels also fell in the PP population (PRT, -1.23 ± 1.08%, P < 0.001; CSII, -0.55 ± 0.90%, P < 0.001); the inter-group difference was again significant and in favor of the PRT group (P < 0.001) (Figure 1).

The probability of failing to comply with agreed-upon sensor wear was not constant among different age cohorts. Analysis according to the age categories proposed by the JDRF (13) revealed highest sensor compliance in the adult age group (>25 years, n=25, sensor wear 74.9% of time), followed by the pediatric population (5-14 years, n=14, sensor wear 68.4% of time). Compliance was lowest in adolescents (15-25 years, n=15, sensor wear 52.4% of time). Due to the small sample size of the age subgroups, no decrease in HbA1c was significantly different compared to the CSII group.

At each visit after treatment initiation, physicians recorded whether patients had modified their treatment regimens. Whereas 20% of patients in the PRT group reported making modifications to their nutritional habits and/or their lifestyle, only 10% of patients in the CSII group did so. In addition, 93.2% of all PRT patients reported using CGM data to adjust their insulin doses, and 59.5% reported that they used CGM data to modify their responses to glycemic excursions.

**Adverse events.** Adverse event (AE) data were collected and analyzed on the safety population. Ten serious adverse events (SAE) were reported: 3 in the PRT group and 7 in the CSII group. Two episodes of ketoacidosis occurred in the PRT group when patients failed to react to the device’s hyperglycemic alarms. One episode of severe hypoglycemia with loss of consciousness also occurred in the PRT group. In this instance, the device was improperly calibrated, and acute alcohol intoxication may have played a role in the AE. Three episodes of ketoacidosis occurred in the CSII group. The overall ketoacidosis rate was 3.2 per 100 patient-years and the overall rate of severe hypoglycemia was 0.64 per 100 patient-years. Four other SAEs occurred in the CSII group that were unrelated to the study devices or the protocol.

**CONCLUSIONS**

Six months after transitioning from MDI to pump therapy, patients with poorly-controlled T1DM achieved significantly improved HbA1c values whether they used a sensor-augmented insulin pump or a conventional pump (the PRT and CSII groups, respectively). The magnitude of improvement within each group was comparable to published data on the efficacy of pump therapy (16), confirming the superiority of pump therapy over MDI in poorly controlled patients.

Among patients who complied with the study protocol, there was a significant between-groups difference favoring the sensor-augmented over the conventional insulin pump. However, when protocol-noncompliant patients were included, the HbA1c improvement was not significant between the PRT and CSII groups.

During the 9-day period between screening and study baseline, the PRT group was trained on sensor use and allowed to modify their MDI dosing regimens based on CGM readings. The observed decrease in
HbA1c levels during this short interval may represent the immediate benefit of exposure to CGM data, even in the absence of an insulin pump. The initial decline in HbA1c levels seen in the PRT group may also explain the blunting of the difference observed between baseline and study end. A more meaningful comparison may therefore be between screening and study end.

MAGE and SD calculations revealed a significantly greater reduction in the PRT group compared to CSII for the entire study population. The improvement in MAGE and SD values was reached without any increase in the number or duration of hypoglycemic events.

Improvements in glycemic control in the PRT group beyond those seen in the CSII group may be attributable to alarms and glucose trend information available to patients during the study, prompting the PRT group to engage in more lifestyle modifications and insulin treatment adjustments.

Recent studies reported that CGM was beneficial in lowering HbA1c. In the GuardControl study (12), HbA1c was reduced by \( > 2\% \) in 26\% of patients after 3 months of continuous sensor use, but not by intermittent use. Hirsch et al. (14) reported that sensor-augmented pump therapy's effectiveness was contingent upon patients' compliance with glucose sensor use. Wearing CGM > 60\% of the time was associated with lowered HbA1c levels. The JDRF study (13) recently showed CGM to improve HbA1c in well-controlled adults with T1DM wearing the continuous glucose sensor at 83\% of the requested time. While sensor compliance was less consistent in other age groups, compliant patients still benefited from the technology (13).

Failure to adhere to many aspects of diabetes management is recognized as an obstacle for successful treatment in adolescents and young adults (17, 18). In the present study, subjects in the 15-24 year-old age group had the highest probability of being noncompliant with the sensor protocol. Our findings support that CGM should be used at least 70\% of the time in order to improve metabolic control when initiating pump therapy, and show that even previously poorly-controlled patients with intensified MDI regimens may realize HbA1c reductions. Patients’ motivation to use CGM as an adjunct to insulin pump therapy is crucial for device effectiveness. Trained health care provider teams should focus on how to adequately select, train, manage and motivate patients in order to optimize benefits from CGM.

This study’s high attrition rate can be considered as a limitation of this trial, and is best explained by the lack of a run-in period which could have selected for the most well-motivated patients. In addition, the short duration of this trial does not provide information on long term impact of the treatment.

In conclusion, patients who use CGM-enabled pumps and who wear sensors at least 70\% of the time realize glycemic benefits beyond those who do not wear sensors or who use conventional insulin pumps. Exposure to CGM data, even before transitioning from MDI to an insulin pump, can lead to HbA1c reductions. Reduction of hyperglycemia without an increased risk of hypoglycemia can be achieved by a combination of modified insulin administration and lifestyle changes.

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Figure Legends

Figure 1: Change in HbA1c during the study period. Panel A, HbA1c levels measured at screening, visits 3, 5 and 6 in the full analysis set (FAS) population. ∆HbA1c inter-group V3/V6: 0.24%, p=0.08; ∆HbA1c inter-group screening/V6: 0.57%, p=0.006.
Panel B, HbA1c levels in the per protocol population (PP), ∆HbA1c inter-group V3/V6: 0.41%, p=0.004; ∆HbA1c inter-group screening/V6: 0.68%, p<0.001. All values are mean ± standard deviation.

Figure 1a. Results Intention-To-Treat – Full study population (n=115): A1c from screening to study end

Figure 1b. Results Per Protocol – ‘Compliant’ patients (n=91): A1c from screening to study end
REFERENCES
1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med 329:977-986, 1993
2. The Diabetes Control and Complications Trial Research Group. Implementation of treatment protocols in the Diabetes Control and Complications Trial. Diabetes Care 18:361-376, 1995
3. Bruttomesso D, Crazzolara D, Maran A, Costa S, Dal Pos M, Girelli A, Lepore G, Aragona M, Iori E, Valentini U, Del Prato S, Tiengo A, Buhr A, Trevisan R, Baritussio A. In Type 1 diabetic patients with good glycaemic control, blood glucose variability is lower during continuous subcutaneous insulin infusion than during multiple daily injections with insulin glargine. Diabet Med 25:326-332, 2008
4. Doyle EA, Weinzimer SA, Steffen AT, Ahern JA, Vincent M, Tamborlane WV. A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. Diabetes Care 27:1554-1558, 2004
5. Pickup JC, Renard E. Long-acting insulin analogs versus insulin pump therapy for the treatment of type 1 and type 2 diabetes. Diabetes Care 31:S140-145, 2008
6. Standards of medical care in diabetes--2009. Diabetes Care 32:S13-61, 2009
7. Latalski M, Jaworska J, Dziemidok P. Frequency of self-monitoring in relation to metabolic control in patients with type I and type II diabetes treated at the diabetic clinic of the Institute of Agricultural Medicine in Lublin. Wiad Lek 55:305-312, 2002
8. Schutt M, Kern W, Krause U, Busch P, Dapp A, Grziwotz R, Mayer I, Rosenbauer J, Wagner C, Zimmermann A, Kerner W, Holl RW. Is the frequency of self-monitoring of blood glucose related to long-term metabolic control? Multicenter analysis including 24,500 patients from 191 centers in Germany and Austria. Exp Clin Endocrinol Diabetes 114:384-388, 2006
9. The DCCT Research Group. Epidemiology of severe hypoglycemia in the diabetes control and complications trial. Am J Med 90:450-459, 1991
10. Bode BW, Schwartz S, Stubbs HA, Block JE. Glycemic characteristics in continuously monitored patients with type 1 and type 2 diabetes: normative values. Diabetes Care 28:2361-2366, 2005
11. Boland E, Monsod T, Delucia M, Brandt CA, Fernando S, Tamborlane WV. Limitations of conventional methods of self-monitoring of blood glucose: lessons learned from 3 days of continuous glucose sensing in pediatric patients with type 1 diabetes. Diabetes Care 24:1858-1862, 2001
12. Deiss D, Bolinder J, Riveline JP, Battelino T, Bosi E, Tubiana-Rufi N, Kerr D, Phillip M. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. Diabetes Care 29:2730-2732, 2006
13. The Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group: Continuous glucose monitoring and intensive treatment of type 1 diabetes. N Engl J Med 359:1464-1476, 2008
14. Hirsch IB, Abelseth J, Bode BW, Fischer JS, Kaufman FR, Mastrocotaro J, Parkin CG, Wolpert HA, Buckingham BA. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technol Ther 10:377-383, 2008
15. Service FJ, Molnar GD, Rosevear JW, Ackerman E, Gatewood LC, Taylor WF. Mean amplitude of glycemic excursions, a measure of diabetic instability. Diabetes 19:644-655, 1970
16. Pickup JC, Sutton AJ. Severe hypoglycaemia and glycaemic control in Type 1 diabetes: meta-analysis of multiple daily insulin injections compared with continuous subcutaneous insulin infusion. Diabet Med 25:765-774, 2008
17. Anderson BJ, Vangsness L, Connell A, Butler D, Goebel-Fabbri A, Laffel LM. Family conflict, adherence, and glycaemic control in youth with short duration Type 1 diabetes. Diabet Med 19:635-642, 2002
18. Insabella G, Grey M, Knafl G, Tamborlane W. The transition to young adulthood in youth with type 1 diabetes on intensive treatment. Pediatr Diabetes 8:228-234, 2007
Table 1. Baseline and demographic characteristics

| Population                        | FAS      | PP        |
|-----------------------------------|----------|-----------|
| Pump Configuration                | PRT      | CSII      | PRT      | CSII      |
| n                                 | 55       | 60        | 32       | 59        |
| Age (mean years [SD])             | 28.1 (15.1) | 28.8 (16.7) | 30.9 (16.2) | 28.1 (15.7) |
| Age ≥ 19 years (n, %)              | 33 (60.0%) | 36 (60.0%) | 21 (65.6%) | 35 (59.3%) |
| Sex (male [n, %])                 | 30 (54.5%) | 34 (56.7%) | 19 (59.4%) | 33 (55.9) |
| Weight (mean kg [SD])             | 65.7 (17.4) | 62.6 (18.6) | 66.8 (19.9) | 62.3 (18.7) |
| Height (mean cm [SD])             | 166.0 (12.3) | 164.6 (14.4) | 166 (13.6) | 164.5 (14.5) |
| BMI (mean kg/m^2 [SD])            | 23.5 (4.1) | 22.5 (4.4) | 23.8 (4.7) | 22.5 (4.4) |
| Screening HbA1c (mean % [SD])     | 9.4 (1.1) | 9.3 (1.1) | 9.2 (1.0) | 9.3 (1.1) |
| Baseline HbA1c (mean % [SD])      | 9.11 (1.28) | 9.28 (1.19) | 8.9 (1.12) | 9.25 (1.19) |
| Baseline MAGE (mg/dl)             | 188.5     | 192.9     | 194.4     | 192.2     |
| Baseline SD (mg/dl)               | 74.4      | 75.1      | 72.1      | 75.1      |
| T1DM duration (mean years [SD])   | 11.2 (9.0) | 12.3 (8.8) | 13.7 (10.2) | 12.2 (8.9) |
| Daily insulin doses(U / day [SD]) | 42.9 (17.5) | 42.2 (17.0) | 40.2 (14.8) | 42.8 (16.5) |
# Table 2. Measured HbA1c, glycemic and insulin parameters changes, baseline to end of study

| Pump Configuration | FAS  |       | PP   |       |
|--------------------|------|-------|------|-------|
|                    | PRT  | CSII  | PRT  | CSII  |
| n                  | 46   | 54    | 30   | 53    |
| Δ Blood glucose (mean mg/dl [SD]) | -30.6 (54.0)** | -10.8 (39.6) | -39.6 (55.8)** | -9.0 (39.6) |
| Δ Hyperglycemia > 190 mg/dl (mean h/d [SD]) | -3.5 (4.8)** | -0.7 (3.8) | -4.1 (5.1)** | -0.6 (3.8) |
| Δ Hyperglycemia AUC (mean mg/dl/d [SD]) | -17.1 (31.7)* | -5.8 (26.7) | -19.1 (35.5)* | -5.2 (26.5) |
| Δ Hyperglycemia (mean episodes/d [SD]) | -0.2 (0.7) | -0.2 (0.7) | -0.2 (0.7) | -0.2 (0.7) |
| Δ Hypoglycemia <70mg/dl (mean h/d [SD]) | 0.3 (1.4) | 0 (1.2) | 0.6 (1.3) | 0.0 (1.2) |
| Δ Hypoglycemia AUC (mean mg/dl/d [SD]) | 0.4 (1.3) | 0.0 (1.8) | 0.7 (1.3) | 0.0 (1.8) |
| Δ Hypoglycemia (mean episodes/d [SD]) | 0.1 (0.9) | 0.1 (0.7) | 0.2 (1.0) | 0.1 (0.7) |
| Δ MAGE (mg/dl)  | -27.5** | -16.2 | -20.4 | -16.2 |
| Δ SD              | -15.8** | -5.7 | -11.3 | -5.7 |
| Δ Daily insulin doses (U/day) | 6.8 * (17.3) | 1.5 (9.1) | 6.2 (14.8) | 1.1 (8.4) |
| Bolus insulin (%/day) | 53.8 (10.0) | 49.8 (15.8) | 53.3 (9.3) | 49.7 (15.9) |
| Number of bolus /day [SD] | 4.7 (1.4) | 3.9 (1.4) | 4.9 (1.4) | 3.9 (1.4) |

*, P ≤ 0.05 vs. CSII group  
**P ≤ 0.005 vs. CSII group
Figure 1a
Results Intention-To-Treat – Full study population (n=115): HbA1c from screening to study end

- ΔHbA1c: -0.57%, p<0.001
- ΔHbA1c: -0.81%, p<0.001
- ΔHbA1c: -1.14%, p<0.001

Figure 1b
Results Per Protocol – ‘Compliant’ patients (n=91): HbA1c from screening to study end

- ΔHbA1c: -0.56%, p<0.001
- ΔHbA1c: -0.95%, p<0.001
- ΔHbA1c: -1.23%, p<0.001