Does Insulin Pump Therapy Have A Role in Type 2 Diabetes?

Bruce W. Bode, MD, FACE
Atlanta Diabetes Associates
Atlanta, Georgia
Disclosures

- Consultant: CellNovo, JNJ, Novo Nordisk, Medtronic, Sanofi, Tandem, Valeritas
- Speaker’s Bureau: Insulet, Lilly, Novo Nordisk, Medtronic, Sanofi
- Grant and Research Support: Lilly, Novo Nordisk, Medtronic, Sanofi, Valeritas
Question 1:

- How many type 2 patients are on the insulin pump in the USA?

a. <25,000
b. 25,000 to 50,000
c. 50,000 to 100,000
d. >100,000
Insulin Therapy Segmentation (US) – 2008

>5.6 Million = 1.2 Million Type 1 (T1)
4.5 Million Type 2 (T2)

Insulin Therapy:

- T1 Conventional: 368,160 (48%)
- T1 MDI: 398,840 (52%)
- T1 Pump Therapy: 361,000
- T2 Conventional: 3,080,160 (69%)
- T2 Pump Therapy: 37,000
- T2 MDI: 1,383,840 (31%)

>31% Penetration in Type 1
<1% Penetration in Type 2

Source: Medtronic with 78% of the market
4.5 Million Type 2 Patients are on Insulin

- Overall, 71% of intensive therapy pts’ **DO NOT** inject outside the home
- 69% of T1 patients **DO NOT** inject outside the home
- 89% of T2 patients **DO NOT** inject outside the home

Source: Roper Starch 2006 (n=2025; T1DM = 105; T2DM = 1,922)
N=790 on Insulin; n=705 insulin injectors; n=85 on pump therapy.
Graph: Type 2 Diabetes Patients only; excludes patients on CSII therapy.
Type 2 Patients Insulin Needs

- Effective (glucose reduction)
- Simplicity
- Discretion (keep disease to themselves)
- Cost effective
- Low risk of hypoglycemia
Normal Daily Plasma *Insulin* Profile

**GOAL** of therapy:
To mimic this physiologic pattern

B=breakfast; L=lunch; D=dinner

Basal/Bolus Treatment Program with Rapid-acting and Long-acting Analogs

Breakfast: Aspart, Lispro or Glulisine
Lunch: Aspart, Lispro or Glulisine
Dinner: Aspart, Lispro or Glulisine

Plasma insulin

Glargine or Detemir
Variable Basal Rate: CSII Program

Plasma insulin

Breakfast  Lunch  Dinner

Bolus  Bolus  Bolus

Basal infusion
Major Suppliers of Insulin Pumps in the US

Animas 2020/One Touch Ping

Roche: Accucheck Spirit

Insulet: Omnipod

Medtronic/Minimed Paradigm 522/722
Current Pump Therapy Indications

- Need to normalize blood glucose (BG)
  - A1C > 6.5% or 7%
  - Glycemic excursions
- Hypoglycemia or Hypoglycemia unawareness
- Need for a flexible insulin regimen

Medicare requires: Fasting C-peptide to be $\leq 110\%$ lower limit of normal
or $\leq 200\%$ lower limit of normal if $\text{CrCl} \leq 50 \text{ ml/min}$ with concurrent $\text{FPG} \leq 225 \text{ mg/dL}$;
or Beta Cell autoantibody positive (+ICA or +GAD antibodies)
T2 CSII Literature Review Summary

- 2 large RCTs comparing CSII vs MDI - no difference in A1C

- 3 smaller RCTs comparing CSII vs MDI - improvement in A1C

- Longitudinal Data with Labrousse-Lhermine et al.
  - n=59
  - Sustained A1c reduction (baseline = 9.45%, 1 year = 7.8%, 2 year = 8.0% and 3 year 8.3%)

- Parkner et al.
  - n= 21
  - Intra subject variability was 41% lower with CSII versus MDI (P = .012)

Parkner et al Insulin and glucose profiles During CSII and long acting insulin. *Diabetic Medicine* 25, 585-591
CSII versus MDI in Type 2 Diabetes
14 Center Randomized Parallel Group Study

Screen:
DM 2 >2 years
On insulin >6 months
A1C > 7.5%;
Stop OHA

Insulin aspart in CSII (n = 66)

Target FBG 80-120 mg/dl

Insulin aspart/NPH in MDI (n = 61)

Dose adjustment

Maintenance period

Week 0    Week 8    Week 24

**CSII versus MDI in Type 2 Diabetes**
**14 Center Randomized Parallel Group Study**

<table>
<thead>
<tr>
<th></th>
<th>CSII</th>
<th>MDI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design:</strong> Multi-center (14) Randomized, parallel group, 24 week study</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>66</td>
<td>61</td>
</tr>
<tr>
<td><strong>Participant age (mean)</strong></td>
<td>55.1 ± 10.2</td>
<td>56.0 ± 8.18</td>
</tr>
<tr>
<td><strong>Years with T2DM</strong></td>
<td>13.8 ± 7.9</td>
<td>11.9 ± 6.4</td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>32.2 ± 4.2</td>
<td>32.2 ± 5.1</td>
</tr>
<tr>
<td><strong>Insulin regimen Inclusion Criteria</strong></td>
<td>1 or more injections</td>
<td></td>
</tr>
<tr>
<td><strong>Insulin treatment years</strong></td>
<td>5.9 ± 5.0</td>
<td>4.6 ± 5.1</td>
</tr>
<tr>
<td><strong>Insulin requirements at enrollment</strong></td>
<td>0.75 ± 0.46 units/kg</td>
<td>0.69 ± 0.39 units/kg</td>
</tr>
<tr>
<td><strong>Insulin in combination with OAD</strong></td>
<td>27</td>
<td>22</td>
</tr>
</tbody>
</table>

MDI = aspart and NPH
CSII = aspart

Raskin P et al. CSII vs MDI in type 2 diabetes *Diabetes Care* 26, 9 2003
CSII versus MDI in Type 2 Diabetes
14 Center Randomized Parallel Group Study

Differences in Glucose Profile and Patient Preference

93% preferred CSII

Difference in 90 min post BF Glucose

Figure 1—Baseline and end-of-study eight-point BG profiles (mean ± SEM) for the intent-to-treat population. Dashed lines represent baseline profiles; solid lines represent end-of-study profiles. ●, means for CSII; □, means for MDI therapy. Number of patients at each time point: CSII, 56–63; MDI, 54–59. *P = 0.02. BB, before breakfast; B90, 90 min after breakfast; BL, before lunch; L90, 90 min after lunch; BD, before dinner; D90, 90 min after dinner; BE, at bedtime.

CSII versus MDI in Type 2 Diabetes
14 Center Randomized Parallel Group Study

Testa et al. Diabetes. 2001;50(suppl 2):1781
CSII vs MDI in Older Adults with Type 2 Diabetes
2 Center Randomized Parallel Group Study

Screen:
DM 2
On insulin
Age > 60yo

Insulin lispro in CSII (n = 53)

Insulin lispro/glargine in MDI (n = 54)

Dose adjustment

Week 0

Week 52

Herman W et al. CSII versus MDI in Older Adults type 2 DM Diabetes Care 28, 7, July 2005
CSII versus MDI in DM 2 patients > age 60 yrs

<table>
<thead>
<tr>
<th></th>
<th>CSII</th>
<th>MDI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Design: 2 center 12 month randomized controlled clinical trial</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>53</td>
<td>54</td>
</tr>
<tr>
<td><strong>Participant age (mean)</strong></td>
<td>66.6 ± 5.9</td>
<td>66.2 ± 4.5</td>
</tr>
<tr>
<td><strong>Years with T2DM</strong></td>
<td>16.9 ± 9.0</td>
<td>15.4 ± 8.9</td>
</tr>
<tr>
<td><strong>BMI (kg/m2)</strong></td>
<td>32.5 ± 5.8</td>
<td>31.8 ± 5.8</td>
</tr>
<tr>
<td><strong>Insulin regimen Inclusion Criteria</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>1 or more injections</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Insulin treatment years</strong></td>
<td>8.1 ± 8.3</td>
<td>8.2 ± 7.7</td>
</tr>
<tr>
<td><strong>Insulin requirements at study end</strong></td>
<td>108 ± 63 units/ day</td>
<td>108 ± 62 units/ day</td>
</tr>
<tr>
<td><strong>Insulin in combination with OAD</strong></td>
<td>23</td>
<td>21</td>
</tr>
</tbody>
</table>

MDI = lispro and glargine
CSII = lispro

Herman W et al. CSII versus MDI in Older Adults type 2 DM *Diabetes Care* 28, 7, July 2005
CSII vs MDI in Older Adults with Type 2 Diabetes
2 Center Randomized Parallel Group Study

Herman W et al. CSII versus MDI in Older Adults type 2 DM Diabetes Care 28, 7, July 2005
Insulin Pump Therapy in Patients with Type 2 Diabetes Safely Improved Glycemic Control Using a Simple Insulin Dosing Regimen

Steven V. Edelman, M.D.,¹ Bruce W. Bode, M.D.,² Timothy S. Bailey, M.D.,³ Mark S. Kipnes, M.D.,⁴ Rocco Brunelle, M.S.,⁵ Xiaoqing Chen, M.S.,⁶ and Juan P. Frias, M.D.⁶

Abstract

Background: This study assessed insulin dose and dosing patterns required to optimize glycemic control with an insulin pump in patients with type 2 diabetes.
Objectives

- To better understand the most effective insulin dosing regimens and the specific pump feature-set required to meet the needs of patients with type 2 diabetes

- To provide data that will help design/power future, larger-scale controlled trials

Edelman et al. *DT&T* 2010: 12(8): 628-33
Pump used in Type 2 DM trial
Study Design

- 16-week, open-label, uncontrolled, multi-center pilot study
- Type 2 DM; Insulin pump naïve (n=60)
- OAs (n=20) or Basal insulin ± OAs (n=20) or MDI ± OAs (n=20)
- A1C 7.0-11.5%

Cohort A:
≥ 2 OAs

Cohort B:
Basal Insulin ± OA(s)

Cohort C:
Basal-Bolus Insulin ± OA(s)

*Animas® 2020 insulin pump
**Insulin glulisine (Apidra®)
# Demographics and Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cohort A (n=18)</th>
<th>Cohort B (n=17)</th>
<th>Cohort C (n=21)</th>
<th>All Cohorts (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>57.3 ± 7.3</td>
<td>55.4 ± 8.3</td>
<td>57.0 ± 12.7</td>
<td>56.6 ± 9.8</td>
</tr>
<tr>
<td>Female (n)</td>
<td>6 (33.3%)</td>
<td>10 (58.8%)</td>
<td>12 (57.1%)</td>
<td>28 (50.0%)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>103.3 ± 20.5</td>
<td>95.6 ± 16.3</td>
<td>97.5 ± 19.9</td>
<td>98.8 ± 19.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34.9 ± 5.1</td>
<td>34.3 ± 4.7</td>
<td>33.8 ± 5.3</td>
<td>34.3 ± 5.0</td>
</tr>
<tr>
<td>DM Duration (y)</td>
<td>10.7 ± 6.2</td>
<td>14.1 ± 6.1</td>
<td>15.1 ± 6.2</td>
<td>13.4 ± 6.3</td>
</tr>
<tr>
<td>A1C (%)</td>
<td>8.2 ± 1.2</td>
<td>8.8 ± 1.5</td>
<td>8.6 ± 1.4</td>
<td>8.5 ± 1.4</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>169 ± 51</td>
<td>170 ± 53</td>
<td>165 ± 58</td>
<td>168 ± 53</td>
</tr>
<tr>
<td>C-Peptide (ng/dl)</td>
<td>3.1 ± 1.6</td>
<td>2.5 ± 1.8</td>
<td>1.7 ± 1.4</td>
<td>2.4 ± 1.7</td>
</tr>
<tr>
<td>Daily Total Insulin Dose (U)</td>
<td>0</td>
<td>31.5 ± 19.7</td>
<td>99.2 ± 65.3</td>
<td>-</td>
</tr>
</tbody>
</table>

All data Mean ± SD

Edelman et al. *DT&T* 2010: 12(8): 628-33
## Baseline Diabetes Therapy

### Insulin Agents

<table>
<thead>
<tr>
<th></th>
<th>Cohort A (n=18)</th>
<th>Cohort B (n=17)</th>
<th>Cohort C (n=21)</th>
<th>All Cohorts (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting Analog</td>
<td>0</td>
<td>17 (100%)</td>
<td>19 (90.5%)</td>
<td>36 (64.3%)</td>
</tr>
<tr>
<td>Rapid-acting Analog</td>
<td>0</td>
<td>0</td>
<td>20 (95.2%)</td>
<td>20 (35.7%)</td>
</tr>
<tr>
<td>Intermediate-Acting</td>
<td>0</td>
<td>0</td>
<td>3 (14.3%)</td>
<td>3 (5.4%)</td>
</tr>
<tr>
<td>Regular Human Insulin</td>
<td>0</td>
<td>0</td>
<td>1 (4.8%)</td>
<td>1 (1.8%)</td>
</tr>
</tbody>
</table>
## Patient Disposition

<table>
<thead>
<tr>
<th></th>
<th>Cohort A</th>
<th>Cohort B</th>
<th>Cohort C</th>
<th>All Cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled (n)</td>
<td>18</td>
<td>18</td>
<td>22</td>
<td>58</td>
</tr>
<tr>
<td>Intent-to-Treat (n)</td>
<td>18 (100%)</td>
<td>17 (94%)</td>
<td>21 (96%)</td>
<td>56 (97%)</td>
</tr>
<tr>
<td>Evaluable (n)</td>
<td>17 (94%)</td>
<td>17 (94%)</td>
<td>20 (91%)</td>
<td>54 (93%)</td>
</tr>
<tr>
<td>Withdrew (n)</td>
<td>1 (5.6%)</td>
<td>1 (5.6%)</td>
<td>2 (9.1%)</td>
<td>4 (6.9%)</td>
</tr>
</tbody>
</table>

2 patients enrolled in the study (Visit 2), but withdrew prior to initiating pump therapy at Visit 3 (Day 1)

Only 2 patients (one from Cohort A and 1 from Cohort B) withdrew from the 16-week study after initiating pump therapy.

Intent-to-Treat (ITT) population: All patients who received at least one dose on insulin via the insulin pump subsequent to Visit 2 (Baseline).
Evaluate population: All ITT patients who completed the study procedures through study termination (Visit 11/Week 16).

Data on file, Animas Corporation
For all cohorts combined (n=56) at Week 16:

- Mean total daily insulin dose was 95±59U (0.93±0.49U per kg) (Mean ± SD)
- Mean ratio of basal-to-bolus insulin was 55% (basal) to 45% (bolus) per day
- ~90% of patients were treated with one (70%) or two (18%) basal rates per day

ITT Population: Cohort A n=18; Cohort B n=17; Cohort C n=21; All Cohorts n=56

Data on file, Animas Corporation
Number of Daily Basal Rates at Week 16

Approximately 90% of patients were treated with 1 or 2 daily basal rates at Week 16.

ITT Population: All Cohorts n=56

Data on file, Animas Corporation
Change in A1C at Week 16

Each cohort had a significant reduction in A1C from baseline (*p<0.001)

- A1C <7.0 and <6.5% achieved by 45% and 28% of patients, respectively
- Change in A1C in patients with baseline A1C >8.5% was -2.1±1.2%

ITT Population: Cohort A n=18; Cohort B n=17; Cohort C n=21; All Cohorts n=56
* All values Mean ± SD, P<0.001 from Baseline

Data on file, Animas Corporation
Change in A1C
All Cohorts (n=56)

Change from Baseline at Wk 16 = -1.2 ± 1.2%
P<0.001

Data on file, Animas Corporation

* All values Mean±SD, P<0.001 from Baseline
ITT Population: All Cohorts n=56
Change in A1C
Patients with Baseline A1C >8.5% (n=23)

ITT Population with A1C >8.5 at Baseline: All Cohorts n=23

Data on file, Animas Corporation
DM 2 Pump Study: Change in A1C and Mean BG based on Baseline Data
Continuous Glucose Monitoring
Percent of Values Within Glycemic Ranges at Baseline and Week 16

Blinded CGM* for 5-7 Days at Baseline and During Week 16

Pre-pump (Baseline)
- <70 mg/dL: 39%
- 70-180 mg/dL: 59%
- >180 mg/dL: 2%

Week 16
- <70 mg/dL: 4%
- 70-180 mg/dL: 69%
- >180 mg/dL: 27%

P <0.05
P <0.001
P <0.001

* DexCom™ SEVEN®

ITT Population: All Cohorts n=56

Data on file, Animas Corporation
### Hypoglycemia

<table>
<thead>
<tr>
<th></th>
<th>Cohort A (n=18)</th>
<th>Cohort B (n=17)</th>
<th>Cohort C (n=21)</th>
<th>All Cohorts (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence of Hypoglycemic AEs</strong></td>
<td>8 (44.4%)</td>
<td>8 (47.1%)</td>
<td>17 (81.0%)</td>
<td>33 (58.9%)</td>
</tr>
<tr>
<td><strong>Incidence of Severe Hypoglycemic AEs</strong></td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Mean (SD) Hypoglycemic episodes per 30 days</strong></td>
<td>0.96 (2.03)</td>
<td>0.95 (1.96)</td>
<td>1.75 (2.70)</td>
<td>1.22 (2.64)</td>
</tr>
</tbody>
</table>

**ITT Population:** Cohort A n=18; Cohort B n=17; Cohort C n=21; All Cohorts n=56
Change in Body Weight at Week 16

- Cohort A: \( \Delta = +0.8 \pm 3.5 \text{ kg} \), \( p=0.4 \)
- Cohort B: \( \Delta = +1.8 \pm 3.6 \text{ kg} \), \( p=0.06 \)
- Cohort C: \( \Delta = +2.8 \pm 2.6 \text{ kg} \), \( p<0.001 \)
- All Cohorts: \( \Delta = +1.9 \pm 3.3 \text{ kg} \), \( p<0.001 \)

Mean ± SD

ITT Population: All Cohorts \( n=56 \)

Data on file, Animas Corporation
Patient Reported Outcomes (DMSRQ/IDSRQ)

Cohort A
- Treatment Satisfaction: $P=0.2$
- Treatment Interference with Daily Activities: $P=0.3$
- Clinical Efficacy: $P<0.005$
- Diabetes Worries: $P=0.2$
- Diabetes Social Burdens: $P=0.4$
- Psychological Well-being: $P=0.8$
- Overall Treatment Preference: $P<0.001$

Cohort B
- Treatment Satisfaction: $P<0.01$
- Treatment Interference with Daily Activities: $P=0.7$
- Clinical Efficacy: $P<0.005$
- Diabetes Worries: $P<0.05$
- Diabetes Social Burdens: $P=0.07$
- Psychological Well-being: $P<0.05$
- Overall Treatment Preference: $P<0.001$

Cohort C
- Treatment Satisfaction: $P<0.001$
- Treatment Interference with Daily Activities: $P=0.4$
- Clinical Efficacy: $P<0.001$
- Diabetes Worries: $P=0.07$
- Diabetes Social Burdens: $P<0.001$
- Psychological Well-being: $P<0.05$
- Overall Treatment Preference: $P<0.001$

ITT Population: Cohort A n=18; Cohort B n=17; Cohort C n=21
Review Article

HIGH-DOSE INSULIN THERAPY: IS IT TIME FOR U-500 INSULIN?

Wendy S. Lane, MD; Elaine K. Cochran, MSN, CRNP; Jeffrey A. Jackson, MD, CDE; Jamie L. Scism-Bacon, PhD; Ilene B. Corey, RN, PNP; Irl B. Hirsch, MD; Jay S. Skyler, MD, MACP

ABSTRACT

Objective: To provide an overview of U-500 regular insulin action, review published clinical studies with U-500 regular insulin, and offer guidance to practicing endocrinologists for identifying patients for whom U-500 regular insulin may be appropriate.

Methods: This review has been produced through a synthesis of relevant published literature compiled via a literature search (MEDLINE search of the English-language literature published between January 1969, and July 2008, related to U-500 insulin resistance, concentrated is described with a treatment algorithm covering dosage requirements ranging from 150 to more than 600 units per day on the basis of the authors’ experience.

Conclusion: Regimen conversion of appropriately selected patients from high-dose, U-100 insulin to U-500 regular insulin therapy on the basis of the recommendations presented in this article may potentially result in improved glycemic control and lower cost. (Endocr Pract. 2009;15:71-79)

Abbreviations:
CSII = continuous subcutaneous insulin infusion; DM
### Table 1
**Reported Clinical Series With U-500 Regular Insulin**

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Study authors</th>
<th>Patients, No.</th>
<th>Study type</th>
<th>Diabetes Type</th>
<th>Method of use</th>
<th>Follow-up duration, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Knee et al (11)</td>
<td>4</td>
<td>Retrospective</td>
<td>Type 2</td>
<td>CSII</td>
<td>6</td>
</tr>
<tr>
<td>2</td>
<td>Garg et al (19)</td>
<td>16</td>
<td>Retrospective</td>
<td>Type 1 and 2</td>
<td>MDI&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3 to 36 (mean 23)</td>
</tr>
<tr>
<td>3</td>
<td>Neal (20)</td>
<td>20</td>
<td>Retrospective</td>
<td>Type 2</td>
<td>TID</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>Wafa and Khan (21)</td>
<td>15</td>
<td>Retrospective</td>
<td>Type 2</td>
<td>SC</td>
<td>12</td>
</tr>
<tr>
<td>5</td>
<td>Lane (12)</td>
<td>9</td>
<td>Retrospective</td>
<td>Type 2</td>
<td>CSII</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>Ballani et al (22)</td>
<td>9</td>
<td>Prospective</td>
<td>Type 2</td>
<td>BID</td>
<td>6</td>
</tr>
<tr>
<td>7</td>
<td>Nayyar et al (23)</td>
<td>81</td>
<td>Retrospective</td>
<td>Type 1 and 2</td>
<td>SC/CSII&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1 to 98 (mean 30)</td>
</tr>
<tr>
<td>8</td>
<td>Bulchandani et al (24)</td>
<td>6</td>
<td>Retrospective</td>
<td>Type 2</td>
<td>CSII&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6</td>
</tr>
</tbody>
</table>

Abbreviations: BID, twice daily; CSII, continuous subcutaneous insulin infusion; MDI, multiple daily injections per reference 12; SC, subcutaneous (frequency of injection unspecified); TID, three times daily.

<sup>a</sup>Actrapid U-500 (Novo Nordisk, Bagsværd, Denmark); other studies used Humulin Regular U-500 (Eli Lilly and Company, Indianapolis, Indiana).

ence, 1.60% [from 10.00% to 8.40%; \( P = .001 \)] and increases in weight (weighted mean difference, 4.2 kg [from 18.8 kg to 123.0 kg; \( P = .002 \))]. Nonsignificant resistance. Severe insulin resistance has been defined as a total daily insulin requirement of 200 units or more in insulin-treated diabetic patients (32). It appears reason-
### Table 2
Comparative Parameters Pre- and Post-U-500 Regular Therapy in Reported Series\(^{a,b}\)

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Patients, No.</th>
<th>Pre HbA(_{1c}), %</th>
<th>Post HbA(_{1c}), %</th>
<th>Pre TDI, units</th>
<th>Post TDI, units</th>
<th>Pre weight, kg</th>
<th>Post weight, kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>10.8 (2.35)(^c)</td>
<td>7.3 (1.34)(^c)</td>
<td>333.8 (199.9)(^e)</td>
<td>213.5 (47.2)(^e)</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>11.34 (3.27)</td>
<td>8.97 (1.89)</td>
<td>313.8 (111.4)(^d)</td>
<td>282.7 (151.6)(^d)</td>
<td>112.7 (31)</td>
<td>119.2 (33.1)</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>9.59 (1.37)</td>
<td>7.83 (1.26)</td>
<td>221.6 (63.3)</td>
<td>214.7 (44.3)</td>
<td>124.8 (27.7)</td>
<td>128.0 (28.8)</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>9.8 (1.8)(^d)</td>
<td>7.6 (1.4)(^d)</td>
<td>219.3 (58.6)(^d)</td>
<td>335 (115.5)(^d)</td>
<td>126.6 (31.5)</td>
<td>128.6 (31.7)</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>8.8 (0.98)</td>
<td>7.67 (0.98)</td>
<td>171.9 (41.9)</td>
<td>166.6 (47.8)</td>
<td>120.28 (38.7)</td>
<td>122.17 (38.6)</td>
</tr>
<tr>
<td>6</td>
<td>9</td>
<td>10.3 (1.9)</td>
<td>7.8 (0.6)</td>
<td>289 (61)</td>
<td>322 (166)</td>
<td>109.9 (26)</td>
<td>114.6 (2.9)</td>
</tr>
<tr>
<td>7</td>
<td>81</td>
<td>10.1 (1.8)</td>
<td>8.9 (2.0)</td>
<td>311 (111.5)</td>
<td>368.4 (179.9)</td>
<td>116.2 (27.1)</td>
<td>121.3 (29.3)</td>
</tr>
<tr>
<td>8</td>
<td>6</td>
<td>9.1 (1.8)</td>
<td>6.9 (0.9)</td>
<td>391 (91)</td>
<td>296 (68)</td>
<td>142.0 (21.8)</td>
<td>139.2 (22.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Weighted mean HbA(_{1c})</th>
<th>Weighted mean TDI</th>
<th>Weighted mean weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10.00</td>
<td>286.0</td>
<td>118.8(^e)</td>
</tr>
<tr>
<td>Weighted mean (\Delta) (post-value minus pre-value)(^f)</td>
<td>-1.60(^%)</td>
<td>+30.9 units</td>
<td>+4.2 kg</td>
</tr>
<tr>
<td>(P) value(^g)</td>
<td>&lt;.001</td>
<td>.17</td>
<td>.002</td>
</tr>
</tbody>
</table>

Abbreviations: HbA\(_{1c}\), hemoglobin A\(_{1c}\); TDI, total daily insulin.

\(^a\) Data are presented as mean (standard deviation).

\(^b\) See Table 1 for further information about studies 1 through 8.

\(^c\) Standard deviations for mean values were calculated from individual patient data in published report.

\(^d\) Additional data provided by written communications with respective authors (Ranjna Garg, MD, April 2008; J. Matthew Neal, MD, April 2008; Mukhtar I. Khan, MD, April 2008)

\(^e\) Available data for these parameters were based on 156 participants.

\(^f\) Weighted mean change was calculated from the study pair differences (post-value minus pre-value) weighted according to the study sample size.

\(^g\) One-sample \(t\) test was used to determine whether the change was significant.
Case 1: Patient CG

- 57 yo female with DM 2 since age 44
- Developed non alcoholic fatty liver disease age 50.
- Placed on pump age 51 for poor control A1C 9.2%
- Received liver transplant age 56
- Control suboptimal; A1C 7.9%
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday 8/23/2010</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuesday 8/24/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wednesday 8/25/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>6.2</td>
</tr>
<tr>
<td>Thursday 8/26/2010</td>
<td></td>
<td></td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friday 8/27/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturday 8/28/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sunday 8/29/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monday 8/30/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuesday 8/31/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wednesday 9/1/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thursday 9/2/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>4.1</td>
</tr>
<tr>
<td>Friday 9/3/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturday 9/4/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sunday 9/5/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Summary</td>
<td>0.0/day</td>
<td>0m</td>
<td>0.9/day</td>
<td>0.0/day</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0.5U</td>
<td>2</td>
<td>5.2U/prime</td>
</tr>
</tbody>
</table>
Case 1: Patient CG

Summary Logbook

Testing, Dosing, and Data Patterns

- Patient tests an average of 0.2 times per day.
- Average number of glucose tests per week is 1.4.
- Average number of glucose tests per week flagged as pre-meal (and/or fasting) is 0.
- Average number of glucose tests per week flagged as post-meal is 0.
- 83.3% of values are hyperglycemic.

<table>
<thead>
<tr>
<th>Date</th>
<th>Overnight</th>
<th>Early Morning</th>
<th>Late Morning</th>
<th>Early Afternoon</th>
<th>Late Afternoon</th>
<th>Early Evening</th>
<th>Late Evening</th>
<th>Bedtime</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/20/2010</td>
<td></td>
<td></td>
<td></td>
<td>203 10:04 AM</td>
<td>132</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/19/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>223 10:28 PM</td>
</tr>
<tr>
<td>Sunday</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/13/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/7/2010</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>288 5:24 PM</td>
</tr>
<tr>
<td>Tuesday</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/4/2010</td>
<td></td>
<td></td>
<td></td>
<td>264 12:11 PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saturday</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Case 1: Patient CG

QUESTION 2:

What would you do?

Options:

a. Send back to CDE/DM training class
b. Place on retrospective/blinded/professional CGM
c. Place on real-time/personal CGM
d. Tell her to monitor her BG 4 times per day
## Case 1: Patient CG

**Adherence (1 of 1)**

### Patient CG

### Glucose Measurements

<table>
<thead>
<tr>
<th></th>
<th>BG Readings</th>
<th>Sensor Duration (h:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuesday</td>
<td>4</td>
<td>24:00</td>
</tr>
<tr>
<td>Wednesday</td>
<td>8</td>
<td>22:30</td>
</tr>
<tr>
<td>Thursday</td>
<td>5</td>
<td>19:05</td>
</tr>
<tr>
<td>Friday</td>
<td>8</td>
<td>19:00</td>
</tr>
<tr>
<td>Saturday</td>
<td>6</td>
<td>23:16</td>
</tr>
<tr>
<td>Sunday</td>
<td>5</td>
<td>21:55</td>
</tr>
<tr>
<td>Monday</td>
<td>4</td>
<td>21:05</td>
</tr>
<tr>
<td>Tuesday</td>
<td>5</td>
<td>21:05</td>
</tr>
<tr>
<td>Wednesday</td>
<td>6</td>
<td>23:46</td>
</tr>
<tr>
<td>Thursday</td>
<td>3</td>
<td>17:45</td>
</tr>
<tr>
<td>Friday</td>
<td>8</td>
<td>10:00</td>
</tr>
<tr>
<td>Saturday</td>
<td>8</td>
<td>24:00</td>
</tr>
<tr>
<td>Sunday</td>
<td>4</td>
<td>23:10</td>
</tr>
<tr>
<td>Monday</td>
<td>7</td>
<td>23:40</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td><strong>5.8/day</strong></td>
<td><strong>12d D5h 50m</strong></td>
</tr>
</tbody>
</table>

### Bolus Events

<table>
<thead>
<tr>
<th></th>
<th>Manual Boluses</th>
<th>Bolus Wizard Events</th>
<th>With Food</th>
<th>With Correction</th>
<th>Overridden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuesday</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Wednesday</td>
<td>1</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Thursday</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Friday</td>
<td>2</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Saturday</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Tuesday</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Wednesday</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Thursday</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Friday</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Saturday</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Sunday</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Monday</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

### Priming Events

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuesday</td>
<td>1</td>
<td>1</td>
<td>0.5</td>
<td>1</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td>Wednesday</td>
<td>1</td>
<td>1</td>
<td>1.0</td>
<td>1</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Thursday</td>
<td>1</td>
<td>1</td>
<td>0.8</td>
<td>1</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

### Data Sources: Minimed Paradigm 722 (331654)
Case 1: Patient CG

Summary by Time of Day

Date Range: Latest 30 days
Include Data by Tag: All

Testing, Dosing, and Data Patterns

- Patient tests an average of 3 times per day.
- Average number of glucose tests per week flagged as pre-meal (and/or fasting) is 0.
- Average number of glucose tests per week flagged as post-meal is 0.
- 32.2% of values are hyperglycemic.
- ADRR: 15

Glucose by Time of Day

[Graph showing glucose levels over time with various markers for flagged values, target ranges, and percentiles.]
Patient CG

24-Hour Glucose Sensor Overlay: Readings & Averages (mg/dL)

Glucose Sensor Overlay Bedtime to Wake-Up and Meal Periods – Readings & Averages (mg/dL)

Bedtime to Wake-up
Bedtime: 10:00 PM – 12:00 AM
Wake-up: 6:00 AM – 9:00 AM

Breakfast: 8:00 AM - 11:00 AM
Meal Activity: 8
Avg Carbs: 28g
Avg Insulin: 8.1U
Avg Carbs/Insulin: 3.4g/U

Lunch: 11:00 AM - 3:00 PM
Meal Activity: 12
Avg Carbs: 28g
Avg Insulin: 7.3U
Avg Carbs/Insulin: 3.9g/U

Dinner: 6:00 PM - 9:00 PM
Meal Activity: 9
Avg Carbs: 28g
Avg Insulin: 7.6U
Avg Carbs/Insulin: 3.7g/U
Case 1: Patient CG

- A1C now 6.3%
- No severe hypoglycemia
- Loves CGM

Recommendations:
- no major changes
- continue to wear CGM
Case 2: 13 yo girl on pump with weight gain

- Diagnosed at age 11: polys without weight loss
- BG 364; trace urine ketones; A1C 10.4%
- Weight 165 pounds; HT 63”
- No family history of DM
- GAD negative; ICA negative
- Placed on pump at age 12 due to A1C 7.9%
Case 2: 13 yo girl on pump with weight gain

- A1C is 6.9% but child now weighs 195 pounds
- Insulin requirement 65 units per day
- What would you do now?
  I chose to check current c-peptide: 4.4 ng/ml

QUESTION #3:
Now what do you do?

a. Pramlintide
b. Metformin
c. GLP-1
d. MNT intervention
Case 2: 13 yo girl on pump with weight gain

- A1C is 6.9% but child now weighs 195 pounds
- Insulin requirement 65 units per day
- Current c-peptide: 4.4 ng/ml
  - Started liraglutide per label; titrated to 1.8 mg/day
  - Returned post 3 months:
    - weight 159 pounds
    - mean BG 93 mg/dl
    - A1C 5.3%
    - off basal; on 1 unit per 10 grams ~11 units per day
    - still on pump: easier to give meal bolus
Future Directions: Meeting the needs

The Start-ups

Valeritas Patch
Debiotech Insulin Nanopump (MEMS)
NiliMEDIX
Starbridge Starlet PATCH
Danfoss Bionics
TheraFuse
NiliMEDIX
Others: M2, SteadyMed, Thomas & Thomas

Medingo
Conclusion 1:
Pump therapy in type 2 diabetes is associated with:
- Improvement in glucose levels
- Improvement in quality of life and satisfaction measures
Conclusion 2:

Further research is needed to determine the appropriate candidates for pump therapy and determine the cost effectiveness of such therapy.