Effectiveness of Sensor-Augmented Insulin Pump Therapy in Type 1 Diabetes

STAR 3 Study

Purpose
- To evaluate improvements in metabolic control in subjects with type 1 diabetes placed on sensor-augmented insulin pump therapy (SAP). These subjects had previously failed to meet glycemic targets with multiple daily injection (MDI) therapy and conventional blood glucose monitoring.

Endpoints
- Change in glycated hemoglobin (A1C) from baseline to 1 year between the two study groups consisting of SAP and MDI.
- Rate of severe hypoglycemia (defined as an episode requiring assistance).

Methods
- This was an unmasked, randomized, controlled trial conducted at 30 diabetes centers in the United States and Canada.
- Subject eligibility criteria: Use of MDI for 3 months, documented self-monitoring of blood glucose (SMBG) 4 times/day for the prior 30 days, 7-70 years of age, type 1 diabetes, and a baseline A1C of ≥7.4% to ≤9.5%. Subjects were required to have access to a computer.
- Subject exclusion criteria: Use of an insulin pump within the previous 3 years, ≥2 severe hypoglycemic events in the year prior to enrollment, use of oral anti-diabetes agents in the previous 3 months, and pregnancy or intent to become pregnant.
- Subjects were randomized to SAP or MDI via block design stratified by site and age group:
  - Adult group: 19-70 years of age
  - Pediatric group: 7-18 years of age
- Prior to randomization, all study subjects received training in insulin diabetes management, carbohydrate counting and correction insulin bolusing. Training for MDI and SAP subjects included use of diabetes management software (CareLink® Therapy Management System for Diabetes-Clinical).
  - The SAP subjects were placed on the MiniMed Paradigm® REAL-Time System (Medtronic) with insulin aspart for 2 weeks before initiating glucose sensor therapy.
  - The MDI subjects used both insulin glargine and insulin aspart.
- All additional scheduled visits following week 5 were the same in both groups.
- Sensor glucose values were collected for 1 week periods at baseline, 6 months and 1 year in both groups. The MDI group used blinded continuous glucose monitoring to collect sensor data.
- Subjects were seen at 3, 6, 9, and 12 months for routine clinic visits.

Results
- 495 patients were randomized; 10 lacked any follow-up A1C values and were not included in the data analysis. Analyses were performed using the intent-to-treat cohort comprised of these 485 subjects.
- There were no significant differences in baseline characteristics between the two study groups except for weight among adults.
- The difference in A1C between study groups favored the SAP group and was statistically and clinically significant in both adult and pediatric subjects.
- In the SAP group, A1C values fell rapidly from baseline to 3 months and remained lower than levels in the MDI group for the rest of the study in both the adult and pediatric groups.
- An increased frequency of sensor use was associated with a greater reduction in A1C values from baseline to 1 year ($p=0.003$).
• There was a non-significant weight increase in the two groups at 1 year.

• Area under the curve (AUC) at 1 year from CGM use was:
  - **Hypoglycemic range** (<70 mg/dL and <50 mg/dL): similar between the two groups with no significant increase from baseline to 1 year.
  - **Hyperglycemic range** (>180 mg/dL and >250 mg/dL): significantly lower in the SAP group

### Mean 1-Year Change in A1C

<table>
<thead>
<tr>
<th></th>
<th>SAP</th>
<th>MDI</th>
<th>Difference</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Subjects (n=485)</td>
<td>- 0.8 ± 0.8%</td>
<td>- 0.2 ± 0.9%</td>
<td>- 0.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adult Group (n=329)</td>
<td>- 1.0 ± 0.7%</td>
<td>- 0.4 ± 0.8%</td>
<td>- 0.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pediatric Group (n=156)</td>
<td>- 0.4 ± 0.9%</td>
<td>+ 0.2 ± 1.0%</td>
<td>- 0.5%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Subjects Achieving A1C Targets at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>Target: ≤7%</th>
<th>ADA TARGETS*</th>
<th>Предметы: 7-19 лет†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Subjects</td>
<td>Adults</td>
<td>Pediatrics 7-18 years</td>
</tr>
<tr>
<td>SAP (n=244)</td>
<td>27% (67)</td>
<td>34% (57) (n=166)</td>
<td>13% (10) (n=78)</td>
</tr>
<tr>
<td>MDI (n=241)</td>
<td>10% (23)</td>
<td>12% (19) (n=163)</td>
<td>5% (4) (n=78)</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.15</td>
</tr>
</tbody>
</table>

* American Diabetes Association (ADA) glycated hemoglobin targets: <8.0% for children 6-12 years; <7.5% for adolescents 13-19 years.
† Post-hoc analysis of study subjects 7-19 years of age achieving ADA targets at 1 year.

### Adverse Events

- There was no statistically significant difference in the rates of either severe hypoglycemia or diabetic ketoacidosis between the study groups.

### Severe Hypoglycemia and Diabetic Ketoacidosis (DKA) at 1 Year

<table>
<thead>
<tr>
<th></th>
<th>SAP (n=247)</th>
<th>MDI (n=248)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Hypoglycemia</td>
<td>number of events (number of subjects)</td>
<td>32 (21)</td>
<td>27 (17)</td>
</tr>
<tr>
<td>number of events per 100 person years</td>
<td>13.31</td>
<td>13.48</td>
<td>0.84</td>
</tr>
<tr>
<td>DKA</td>
<td>number of events (number of subjects)</td>
<td>3 (3)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Adapted from study.

### Conclusions

- The decrease in A1C levels in the SAP group was achieved at 3 months and sustained throughout the 1 year study.
- The improvement in A1C levels was achieved without an increase in the rate of severe hypoglycemic events and without an increase in the time spent at an AUC <70 mg/dL.
- A significantly greater number of adults and pediatric subjects in the SAP group reached ADA age specific A1C targets.