Effectiveness of Sensor-Augmented Pump Therapy in Children and Adolescents with Type 1 Diabetes in the STAR 3 Study

Study Objective
- To compare the effects of sensor-augmented pump (SAP) therapy to multiple daily injection (MDI) therapy in pediatric patients.

Endpoints
- Change in glycated hemoglobin (A1C) from baseline to 1 year in the 2 treatment arms.
- Other outcome measures included percent of patients reaching age-specific A1C goals in each treatment arm, sensor compliance and various measures of glycemic variability.

Methods
- Subjects aged 7-18 years of age were randomized separately from subjects aged 19-70 years of age to either SAP therapy with insulin aspart or MDI using insulin aspart and insulin glargine. Subjects randomized to MDI were placed on individualized regimens by their respective investigator-physicians. All subjects were trained on the use of CareLink® therapy management software for diabetes.
- Quarterly visits provided individual therapy optimization and for A1C measurements. Training and visit schedules were identical after the first 5 weeks, during which SAP patients completed device training.
- All subjects completed blinded baseline CGM studies. CGM studies were also performed at 6 and 12 months for all subjects, the MDI group was blinded to the results.
- The complete study design has been reported elsewhere.

Results
- At baseline, mean A1C levels in children (7-12 years of age) and adolescents (13-18 years of age) were 8.20±0.54% and 8.37±0.53%, respectively (p=0.054) Subjects assigned to the different treatment arms were well matched for age, A1C, BMI and duration of diabetes.
- Statistically significant differences favoring the SAP group were seen at all post-baseline visits in children and adolescents (all p<0.05).
- Children in the SAP group improved their A1C values by 3 months and maintained these improved values throughout the study. Children receiving MDI maintained baseline A1C values. See Figure A.
- The A1C reduction seen in adolescents in the SAP group at 3 months was not maintained. Adolescents in the MDI group were at risk for worsening A1C levels as the study progressed. See Figure B. At the end of the 12-month study, the adolescents in the SAP group continued to demonstrate a reduction in A1C, although not as significant as at month 3), vs. the MDI group will showed an increase in A1C by study end.
- The percent of at-goal subjects at each visit was consistently higher in the SAP group in both age cohorts. Children were consistently more likely to meet their goal of <8% than adolescents were to reach their goal of <7.5% (p<0.01).
  - 88% (38 of 43) of children in the SAP group had reached their A1C goal at either month 3 or 6, compared with 51% (20 of 39) in the MDI group.
  - 57% (20 of 35) of adolescents in the SAP group had reached their A1C goal at least once by month 6, compared with only 13% (5 of 39) of adolescents in the MDI group.
Results (cont’d)

- Over the entire 12-month study, sensor use was higher in children than in adolescents (p=0.025).
  - Children and adolescents wore sensors 62% and 63% of the time, respectively during the first three months of the study. Median wear for quarters 2-4 was at least 63% for children and no more than 55% for adolescents.
  - Sensor use was always higher in subjects meeting A1C goals than in those who did not meet their goals (p=0.03[Q1], p=0.008[Q2], p=0.04[Q3], p=0.03[Q4]). Over 1 year, the difference in sensor compliance was highly significant for those meeting vs. not meeting A1C goals (62 vs. 46%, respectively; p<0.001). This difference held up for both children (p=0.002) and adolescents (p=0.014).
- Mean area under the curve (AUC) values for both hypo- and hyperglycemic exposure were similar in the 2 treatment groups at baseline. At 1 year, subjects in the SAP group had significantly lower hyperglycemic exposure than subjects in the MDI group at levels of either 180 mg/dL or 250 mg/dL. Also at 1 year, there was no significant between-group difference in hypoglycemic exposure at either 70 mg/dL or 60 mg/dL.
- Glycemic variability was measured by using the standard deviation of sensor glucose values (SD score). Mean amplitude of glycemic excursions (MAGE) was also calculated.
  - A highly significant between group SD-score difference favoring the SAP group was evident in both the children and adolescent cohorts at 1 year.
  - There was a statistically significant difference in the between-group MAGE favoring the SAP group among adolescents (p=0.01) but not in children (p=0.21).
- Results for all subjects have been reported elsewhere.2

### Quarterly Mean (±SEM) A1C levels in Subjects Aged 7-12 yrs and 13-18 yrs*

<table>
<thead>
<tr>
<th>Month</th>
<th>Age 7-12</th>
<th></th>
<th>Age 13-18</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>8.5</td>
<td>A1C (%)</td>
<td>8.0</td>
<td>MDI</td>
</tr>
<tr>
<td>3</td>
<td>8.6</td>
<td>SAP</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>8.4</td>
<td></td>
<td>8.0</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>8.3</td>
<td></td>
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<tr>
<td>12</td>
<td>8.2</td>
<td></td>
<td>8.0</td>
<td></td>
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</tbody>
</table>

*Ages at time of enrollment in study

**Authors’ Conclusions**

- In the SAP group, A1C reductions were generally attributable to reductions in hyperglycemia, which may explain why lowering A1C did not increase the risk of severe hypoglycemic events as has been reported in other studies.3
- The ability of our patients to adopt sensor and pump technologies rapidly enough to achieve nadir A1C levels by 3 months and to maintain lower A1C levels compared with the MDI group is noteworthy.
- SAP therapy allows children and adolescents with inadequately controlled type 1 diabetes to reduce A1C values, hyperglycemic excursions, and glycemic variability in a rapid, sustainable and safe manner.
