Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) Study

Results from the 6-month continuation phase

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OBJECTIVE—To examine the effects of crossing over from optimized multiple daily injection (MDI) therapy to sensor-augmented pump (SAP) therapy for 6 months, and the effects of 18 months' sustained use of SAP.

RESEARCH DESIGN AND METHODS—The 6-month, single-crossover continuation phase of Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) provided SAP therapy to 420 subjects who completed the 1-year randomized study. The primary outcome was change in A1C in the crossover group.

RESULTS—A1C values were initially lower in the continuing-SAP group than in the crossover group (7.4 vs. 8.0%, $P < 0.001$). A1C values remained reduced in the SAP group. After 3 months on the SAP system, A1C decreased to 7.6% in the crossover group ($P < 0.001$); this was a significant and sustained decrease among both adults and children ($P < 0.05$).

CONCLUSIONS—Switching from optimized MDI to SAP therapy allowed for rapid and safe A1C reductions. Glycemic benefits of SAP therapy persist for at least 18 months.

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The sensor-augmented pump (SAP) system combines insulin pump and continuous glucose monitoring (CGM) technologies, and its efficacy was studied in the 1-year randomized phase of the Sensor-Augmented Pump Therapy for A1C Reduction (STAR 3) study (1). Compared with subjects on multiple daily injections (MDI), those on SAP experienced greater reductions in A1C levels by 3 months, and this advantage persisted for the entire study (2). An optional continuation phase allowed MDI subjects to switch to SAP therapy for 6 months (the crossover group) and allowed SAP subjects to remain on uninterrupted SAP therapy (the SAP group) for a total of 18 months. We examined the effectiveness of SAP therapy in subjects transitioning from previously optimized MDI therapy and the durability of glycemic benefits in the SAP group over 18 months.

RESEARCH DESIGN AND METHODS—STAR 3 eligibility criteria included type 1 diabetes, age 7–70 years, use of MDI with a long-acting insulin analog, A1C between 7.4 and 9.5%, and less than two severe hypoglycemic events (3) in the previous year. Subjects were randomized to receive SAP (Paradigm REAL-Time System, Medtronic MiniMed, Inc., Northridge, CA) with insulin aspart or to MDI using insulins aspart and glargine. Therapy was optimized individually, and A1C was obtained at quarterly visits. Subjects beginning SAP therapy received training for pumps, CGM sensors, and therapy management software. All subjects in the continuation phase were supplied with sensors and encouraged to wear them regularly. The primary efficacy measure was the change in A1C from 12 to 18 months in both treatment groups; the primary safety measure was the difference in the rates of severe hypoglycemia. The study Consolidated Standards of Reporting Trials (CONSORT) diagram and statistical methods are given in the Supplementary Material.

RESULTS—A total of 420 of 443 subjects completed the study phase and participated in the continuation phase; 204 of 216 SAP subjects (94%) and 190 of 204 crossover subjects (93%) completed both phases of the study. In the SAP group, the improvement in A1C levels seen during the study phase was maintained during the continuation phase (Fig. 1*A*). Overall mean (± SEM) A1C levels for these subjects at 15 and 18 months were not significantly different than the 12-month value of 7.4 ± 0.1% ($P > 0.05$). In contrast, patients in the crossover group realized a significant decrease in A1C from 12 months (8.0 ± 0.1%) to 15 or 18 months (7.6 ± 0.1%, $P < 0.001$; Fig. 1*A*). The significant decrease in A1C values in the crossover group was seen in adult (n = 141; Fig. 1*B*) and pediatric (n = 63; Fig. 1*C*) subjects.

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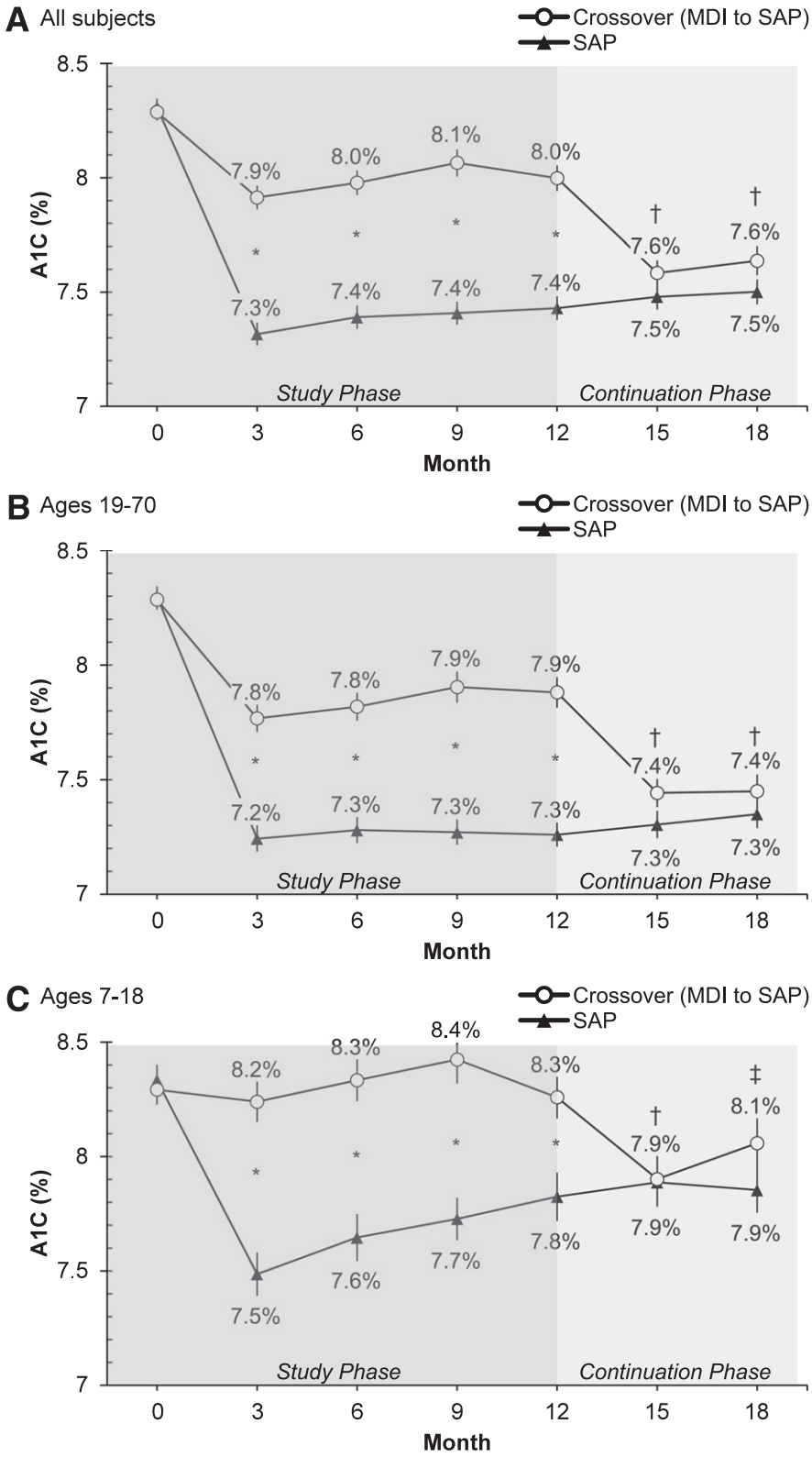

Figure 1—*Mean (± SEM) A1C values of 420 subjects who entered the STAR 3 continuation phase. All subjects in the continuation phase used SAP therapy.* A*: All subjects (MDI,* n *= 204; SAP,* n *= 216).* B*: Adult subjects (MDI,* n *= 141; SAP,* n *= 151).* C*: Pediatric subjects (MDI,* n *= 63; SAP,* n *= 65).* *P *< 0.001 for between-groups comparison;* †P *< 0.001 and* ‡P *< 0.05 for within-group comparison using the crossover group's 12-month A1C value as the comparator.*

Subjects in the SAP group were able to maintain their A1C levels if CGM sensors were used >40% of the time; subjects who used sensors less frequently experienced slight deteriorations in glycemic control. In the crossover group, maximum improvements in A1C were observed with sensor wear times >60% (Supplementary Table 1). Mean sensor wear times in the continuation phase were greater among adults (61 ± 24% of the time) than among pediatric subjects (45 ± 24% of the time; $P < 0.001$). Rates of severe hypoglycemia were not significantly different among the SAP and crossover groups in the continuation phase (2.8 vs. 1.0%, respectively; $P > 0.05$; Supplementary Table 2).

CONCLUSIONS—The STAR 3 continuation phase results support and extend the findings of the study phase. In the study phase, A1C levels were lowered by ~0.5 to 0.6% more with SAP treatment than with MDI. The current data show that a similar degree of improvement in A1C levels was achieved when subjects switched from MDI to SAP after a 12-month period of optimized MDI therapy. Maximal lowering of A1C levels was associated with CGM sensor wear times of >60% in the crossover group; this was similar to wear times associated with maximal A1C lowering in the SAP group during the randomized study phase.

The improved A1C levels achieved by the SAP group during the first 12 months of the study were maintained at 15 and 18 months. Sensor wear times of >40% were required during the continuation phase for experienced SAP users to maintain the A1C benefits achieved during the study phase.

Age-dependent patterns of response in crossover adult and pediatric subjects during the continuation phase were similar to those observed during the study phase. Pediatric patients used their sensors less frequently than adults, and lower wear times were associated with a smaller reduction in A1C levels. A separate analysis of STAR 3 data comparing children and adolescents showed additional age-dependent differences in outcomes and behaviors (4).

Participants were fully aware of the devices they were using and may have been motivated to use the SAP system appropriately. Because the study only enrolled subjects with type 1 diabetes with initial A1C values of 7.4–9.5% and only included 2 treatment arms, its generalizability may be limited. The benefits of pump therapy with or without real-time CGM have been recently compared (5). Work continues

toward the integration of SAP platforms and controller algorithms that can safely reduce hypoglycemic exposure (6) and may someday provide fully closed-loop insulin delivery (7).

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