

DIABETES CLINICAL SUMMARIES



SWITCH (2012): BENEFIT OF SAP VS CSII

STUDY RATIONAL

- Sensor Augmented Pump (SAP) therapy is the combination of Continuous Subcutaneous Insulin Infusion (CSII) and Continuous Glucose Monitoring (CGM). SAP has been proven to significantly decrease HbA1c, without increasing hypoglycaemia, compared to Multiple Daily Injections (MDI)¹.
- Whether patients with inadequately controlled type 1 diabetes on CSII therapy can achieve improved metabolic control with the addition of Continuous Glucose Monitoring (CGM) remained to be established.

OBJECTIVES

- The study aimed to evaluate the clinical effectiveness of Sensor Augmented Pump (SAP) therapy in the reduction of HbA1c as compared to CSII, in Type 1 diabetes.

DESIGN AND METHODS

- The study was a randomised controlled crossover trial comparing SAP therapy vs CSII therapy over two periods of 6 months.
- Subjects eligibility criteria: Type 1 diabetes for ≥ 1 year; aged 6 to 70; on CSII therapy for ≥ 6 months; no previous experience with CGM; HbA1c level between 7.5% and 9.5%.
- Enrolled subjects were trained on the insulin pump and glucometer that would be used during the study and wore the system during a 1-month run-in period.
- Subjects were randomised to SAP therapy, adding CGM (Sensor On/Off group), or to continue with CSII therapy (Sensor Off/On group) for 6 months. After a 4-month washout period, aimed to minimise possible carry-over effects, subjects crossed over to the other therapy for 6 months (Figure 1). Adults and children were randomised separately to ensure a proper balance in each group.
- Study visits occurred every 6 weeks during the treatment periods where the data from all devices were uploaded to CareLink™ Therapy Management System. No visit occurred during the washout period.
- The primary endpoint was the difference in HbA1c levels between the Sensor On and Sensor Off arms after 6 months of follow-up, adjusting for baseline levels.
- Secondary endpoints were the mean difference in the time spent in hypoglycaemia (< 3.9 mmol/L), hyperglycaemia (> 10 mmol/L) and euglycaemia (3.9-10 mmol/L) which was measured during the last two weeks of each treatment period with blinded CGM (Figure 1).
- Subjects on SAP therapy were encouraged to make self-adjustments to their treatment using real-time CGM values.

KEYPOINTS

- 0.43% lower HbA1c with SAP
- Larger HbA1c difference when sensor is used $> 70\%$ of the time (-0.51%)
- 38.7% reduction in hypoglycaemia
- 18.9% reduction in hyperglycaemia
- 15.7% increase in euglycaemia
- Removal of CGM resulted in a loss of metabolic benefit

STUDY TYPE

- Randomised Controlled Crossover Trial
- SAP vs CSII
- 2 periods of 6-month treatment
- 153 subjects (aged 6 – 70)

ENDPOINTS

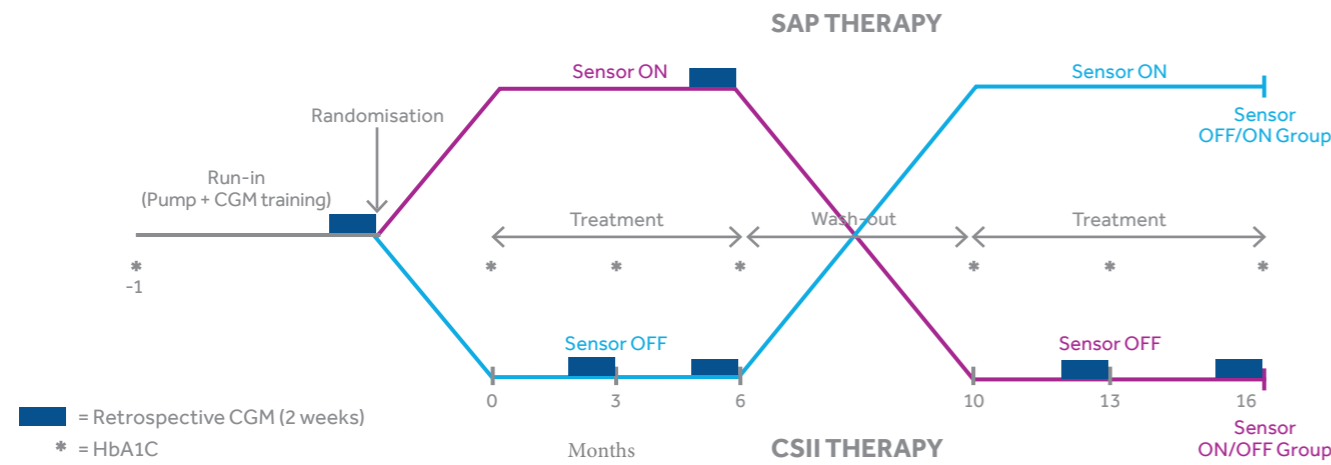
- Difference in HbA1c levels between Sensor On and Sensor Off after 6 months of follow-up, adjusting for baseline levels
- Time spent in hypoglycaemia (< 3.9 mmol/L)
- Time spent hyperglycaemia (> 10 mmol/L)
- Time spent in euglycaemia (3.9-10 mmol/L).

REFERENCE

The use and efficacy of continuous glucose monitoring in type 1 diabetes treated with insulin pump therapy: a randomized controlled trial. Battelino T. et al. Diabetologia 55:3155-3162, 2012.



FIGURE 1: Study Design



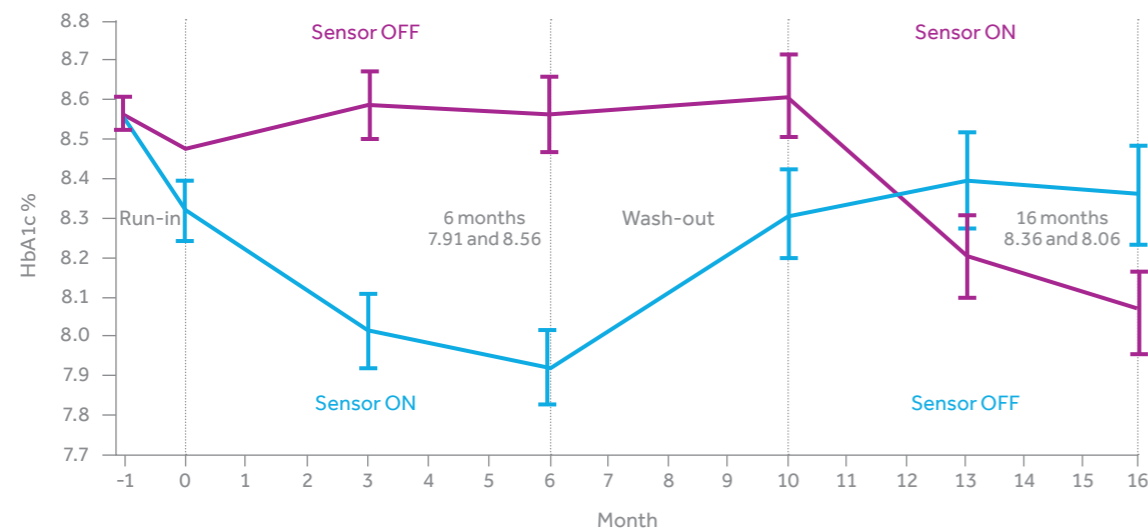
RESULTS

153 subjects were randomised to either the Sensor OFF/ON Group (77 subjects) or the Sensor ON/OFF Group (76 subjects).

HbA1c levels

- At the end of both treatment periods the mean HbA1c level was 8.04% with SAP therapy and 8.47% with CSII therapy. This represents a mean difference of 0.43% ($p < 0.001$) in favour of the SAP therapy. The mean difference in HbA1c levels was 0.46% ($p < 0.001$) and 0.41% ($p < 0.001$) in paediatrics and adults, respectively (Figure 2).
- The HbA1c level decreased continuously during the 6-month of SAP therapy. Discontinuation of the sensor resulted in HbA1c level reverting towards baseline level during the 4-month washout period.

FIGURE 2: Mean HbA1c values



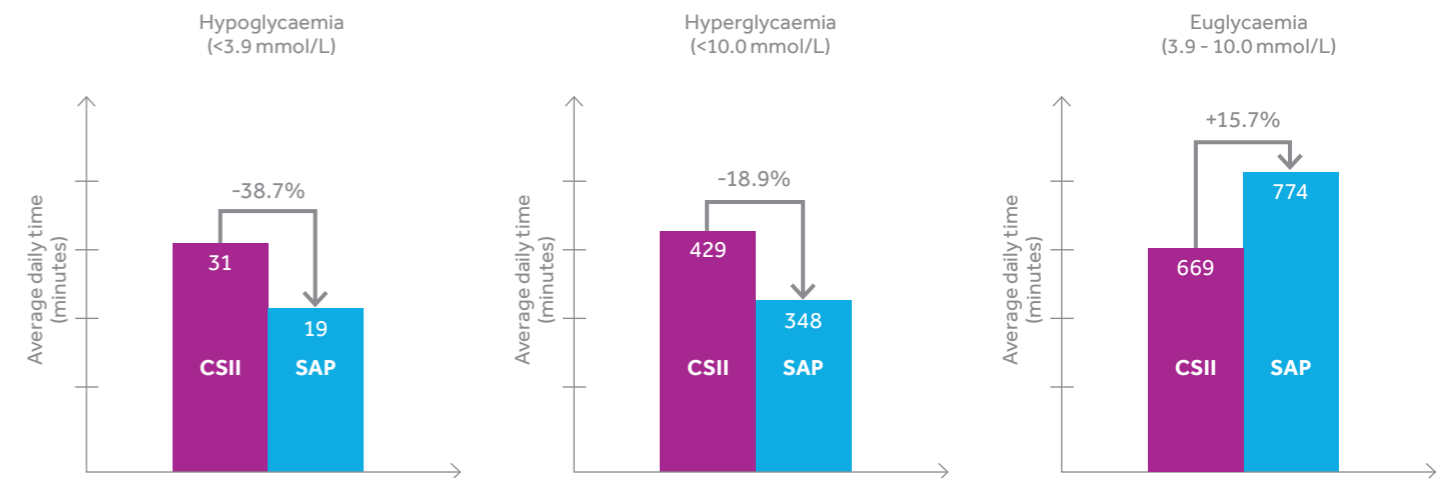
Impact of sensor usage

- The mean sensor usage was 80% of the time. 72% of the subjects used the sensor $\geq 70\%$ of the time and 24% used the sensor $> 90\%$ of the time.
- The HbA1c difference was larger in the group that used the sensor $\geq 70\%$ of the time (0.51%, $p < 0.001$) than in the group that used the sensor $< 70\%$ of the time (0.24%, $p < 0.03$).

Sensor Glucose Values

- The average daily glucose level was significantly lower with SAP therapy compared to CSII therapy (8.82 vs 9.44 mmol/L, $p < 0.001$).
- Time spent in hypoglycaemia (< 3.9 mmol/L) was reduced by 38.7% with SAP therapy compared to CSII therapy (19 vs 31 min/day, $p = 0.009$).
- Time spent in hyperglycaemia (> 10 mmol/L) was also reduced by 18.9% (348 vs 429 min/day, $p < 0.001$) and time spent in euglycaemia (3.9–10 mmol/L) was increased by 15.7% (774 vs 669 min/day, $p < 0.001$).

FIGURE 3: Sensor Glucose values



Treatment patterns

- The mean number of daily boluses was significantly greater with SAP therapy than compared to CSII therapy (6.8 vs 5.8, $p < 0.0001$).
- The mean number of daily temporary basal rates (0.75 vs 0.26, $p < 0.0001$) and the daily use of the manual basal suspend function (0.91 vs 0.70, $p < 0.018$) were also significantly higher with SAP therapy compared to CSII therapy.

CONCLUSIONS

- SAP therapy was associated with decreased HbA1c levels compared to CSII therapy and when CGM was discontinued HbA1c reverted toward baseline level.
- Using sensor >70% of the time provides a larger HbA1c decrease.
- SAP therapy was associated with significant decrease in time spent in both hypoglycaemia and hyperglycaemia, and significant increase in time spent in euglycaemia.
- More frequent self-adjustments of insulin therapy based on real-time CGM data may have contributed to these effects.

Additional References

1. Effectiveness of Sensor-Augmented Insulin Pump Therapy in Type 1 Diabetes. Bergenstal RM, et al. N Engl J Med 363:311-20, 2010.