Medtronic

Insulin pump treatment compared with multiple daily injections for treatment of type 2 diabetes (OpT2mise): a randomised open-label controlled trial

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Purpose

• To compare the efficacy and safety of pump therapy and multiple injection therapy in patients with type 2 diabetes who had not responded to a basal-bolus regimen after active insulin titration.
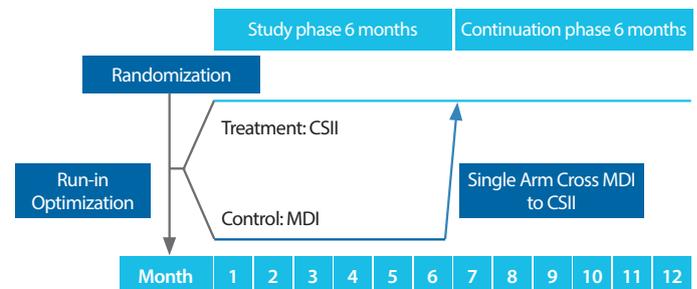
Endpoints

• The primary endpoint of the study was to evaluate the difference in average HbA1c change (baseline to 6 months) between the pump therapy CSII and MDI group.

• The secondary endpoints of the study included:
 - Between group change in glycemic variability parameters , assessed by blinded continuous glucose monitoring
 - Number of severe hypoglycemic events and diabetic Ketoacidosis events
 - Change in Insulin dosage between baseline and 6 months
 - Change in lipid parameters, weight and blood pressure between baseline and 6 months

Methods

• This study was a multicenter, randomized, controlled trial conducted at 36 Diabetes center in Europe, Israel, Canada, South Africa and in the United States.

• Patients underwent a 8 week run in phase, considered as a last attempt to improve and achieve optimal injection therapy, including education and insulin intensification to >0.7U/kg/day.

• Subject eligibility criteria :

 - Run in phase: Type 2 Diabetes patient with HbA1c between 8.0% and 12%, MDI users for at least 3 months with ≥3 injections/day (basal/bolus therapy) and with insulin requirements from 0.5 to 1.8 U/kg/day

 - Randomization: Type 2 patients HbA1c ≥ 8.0% and ≤12% despite insulin intensification, with insulin requirements from 0.7 to 1.8 U/kg/day and having performed at least 2.5 blood glucose measurement per day during the run-in phase.

Study schedule

| Study phase 6 months | Continuation phase 6 months |

Randomization

Treatment: CSII

Run-in Optimization

Control: MDI

Single Arm Cross MDI to CSII

| Month | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |

• Randomization occurred in a 1:1 ratio to continue injection therapy for 6 months or to receive pump therapy with the MiniMed insulin pump

• Pump training of the patient was performed according to site routine practice

• Subjects randomized to MDI continued titration to achieve glycemic control

• Blinded continuous glucose monitoring values were collected for 1 week period at baseline, and at 6 months in both groups

• Subject were seen at 1, 2, 3 and 6 months for study visits and were offered identical support from healthcare providers

• After completion of the study phase, patients receiving multiple injections were switched to pump therapy and follow up was continued for a further 6 months

Results

• A total of 495 patients entered in the 8-week run-in phase and 331 were randomized in the study ; 168 subjects were assigned to the pump therapy group and 163 were assigned to the MDI group, which continued using multiple daily injection

• Post randomisation, 23 patients withdrew from the study and 308 completed the study phase

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HbA1c

- There was an overall 1.1% reduction in the CSII group with a significant 0.7 % between group difference in favor of CSII from baseline to 6 months

- At the end of the study, 55% of subjects in the CSII group had achieved HbA1c values of <8%, compared to 28% of subjects in the MDI group.

- Subjects in the highest tertile of baseline HbA1c (baseline HbA1c between 9.2 and 11.5%) realized the largest between-groups difference in HbA1c at 6 months (-1.1 ± 1.4%).

Change in HbA1c - 6 months
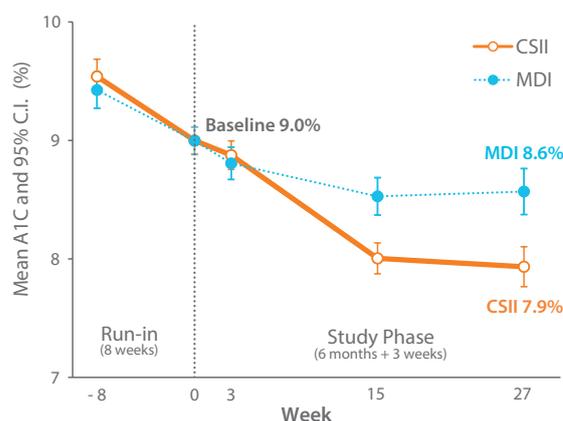
Continuous Glucose monitoring data

Based on blinded CGM data collected over 6 days at baseline and at the end of the study phase, subjects in the pump therapy group experienced significantly greater reductions in mean glucose levels than subjects in the MDI group, with no significant changes in time spent in hypoglycemia.

|	CSII	MDI	(CSII – MDI)
Change in 24-h mean glucose level (mg/dL)	-23.0 ± (42.6)	-5.9 ± (30.2)	-17.1*
AUC change >180 mg/dL (mg/dL × min)	-11.5 ± (25.5)	-2.2 ± (15.8)	-9.3*
Change in time spent >180 mg/dL (min / 24 h)	-225.6 ± (355.9)	-56.8 ± (256.3)	-168.7**
AUC change <70 mg/dL (mg/dL × min)	0.0 ± (0.6)	-0.1 ± (0.9)	0.1
Change in time spent <70 mg/dL (min / 24 h)	8.8 ± (49.6)	5.1 ± (71.0)	3.7

*, $p < 0.01$; **, $p < 0.001$
Values for continuous variables given as mean+/- (SD)

Insulin dosage and SMBG

- The total daily dose of insulin required in the CSII group decreased during the study and was 20.4% lower than in the MDI group at the end of the study phase.

Insulin requirements
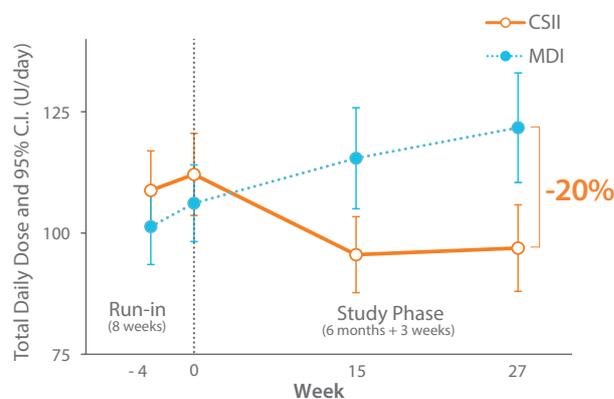
Lipid parameters, weight and blood pressure

- Lipid parameters did not change significantly during the study, with the exception of HDL cholesterol, which increased by 8% in CSII group while decreasing by 7% in the control group

- No significant difference in blood pressure nor weight was observed in the study between the 2 groups

Safety

- One episode of severe hypoglycemia occured in the control group and there were no episode of ketoacidosis in both study groups

Conclusion

- In patients with sub-optimally-controlled type 2 diabetes, pump therapy significantly improved glycaemic control, compared with injection therapy, with lower insulin doses and maintained safety.

- The present study opens new treatment options for those patients failing on current injection regimens, and suggests that pump therapy may therefore be considered a valuable therapeutic option in this population