

**The RealTrend study: effect of continuous glucose monitoring on metabolic control in addition to pump therapy in poorly controlled type 1 diabetic patients**

D. Raccach<sup>1</sup>, V. Sulmont<sup>2</sup>, Y. Reznik<sup>3</sup>, B. Guerci<sup>4</sup>, E. Renard<sup>5</sup>, H. Hanaire<sup>6</sup>, N. Jeandidier<sup>7</sup>, M. Nicolino<sup>8</sup>;

<sup>1</sup>University Hospital Sainte Marguerite, Marseille, <sup>2</sup>University American Memorial Hospital, Reims, <sup>3</sup>University Cote de Nacre Hospital, Caen, <sup>4</sup>University Hospital Jeanne d'Arc, Nancy, <sup>5</sup>University Hospital Lapeyronie, Montpellier, <sup>6</sup>University Hospital Ranguel, Toulouse, <sup>7</sup>University Hospitals, Strasbourg, <sup>8</sup>Pediatric Endocrinology, University Hospital Debrousse, Lyon, France.

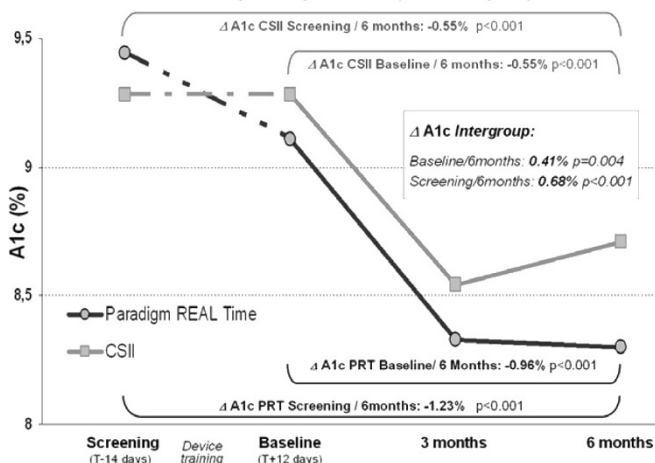
**Background and aims:** Efficacy of insulin pump augmented with continuous glucose monitoring (CGM) versus Continuous Subcutaneous Insulin Infusion with standard self-monitoring of blood glucose has not yet been determined.

**Materials and methods:** In this randomized, controlled, multi-center trial, 132 adults and children with type 1 diabetes, insufficiently treated with multiple daily insulin injections (A1c ≥ 8%) were assigned to a 6 months treatment in one of 2 study arms: PRT arm, fitted with the Paradigm REAL Time System (Medtronic insulin pump with integrated CGM), or CSII arm, fitted with an insulin pump and conventional blood glucose self-monitoring. In the PRT arm, patients wore glucose sensors for 9 training days prior to baseline HbA1c. HbA1c change between baseline and study end served as a primary endpoint in the 2 study arms. Secondary endpoints included hyper- and hypoglycemia parameters measured by CGM: average glucose, time spent above and below hyper- and hypoglycemia limits, and respective area under the curve.

**Results:** HbA1c was analyzable for 115 patients (46 children, 69 adults) of the full analysis population (FAS) and improved between baseline and study end in the two groups (PRT, n=55, -0.81%±1.09; CSII, n=60, -0.57%±0.94; p=0.087). A per protocol (PP) analysis of 91 patients (35 children, 56 adults) who wore sensors over 70 % of the time (as required by the inclusion criteria) showed a significant difference in A1c reduction between groups (PRT; n=32; -0.96%±0.93, CSII, n=59; -0.55%±0.93, p=0.004). Ancillary analyses revealed a significant decrease in HbA1c levels between the screening visit and the end of the study (PRT -1.14±1.21, p<0.001; CSII group -0.57±0.91, p<0.001), as well as a significant difference in favor of the PRT group (p=0.006) for the entire study population as well for the per protocol population (PRT -1.23±1.08, p<0.001; CSII -0.55±0.90, p<0.001; inter-group comparison: p<0.001). In PRT group, CGM hyperglycaemia parameters decreased in line with HbA1c, without increased hypoglycaemia.

**Conclusion:** In both FAS and PP populations HbA1c decreased in both study arms after treatment was changed from MDI to CSII or PRT, but improved significantly more in the PRT group when patients wore the CGM more than 70% of the time versus CSII.

**A1c reduction in compliant patients (PP analysis)**



**Sensor augmented pump therapy substantially lowers HbA<sub>1c</sub>; a randomized controlled trial**

J. Hermanides<sup>1</sup>, K. Norgaard<sup>2</sup>, D. Bruttomesso<sup>3</sup>, C. Mathieu<sup>4</sup>, A. Frid<sup>5</sup>, C.M. Dayan<sup>6</sup>, P. Diem<sup>7</sup>, C. Fermon<sup>8</sup>, I.M.E. Wentholt<sup>1</sup>, J.B.L. Hoekstra<sup>1</sup>, J.H. DeVries<sup>1</sup>;

<sup>1</sup>Academic Medical Centre, Amsterdam, Netherlands, <sup>2</sup>Hvidovre Hospital, Denmark, <sup>3</sup>University of Padova, Italy, <sup>4</sup>Catholic University Leuven, Belgium, <sup>5</sup>Malmö University Hospital, Sweden, <sup>6</sup>University of Bristol, United Kingdom, <sup>7</sup>University of Bern-Inselspital, Bern, Switzerland, <sup>8</sup>Lille University Hospital, France.

**Background and aims:** An insulin pump augmented with a continuous glucose monitor (CGM) and mealtime insulin dose advisor is the first step towards a closed-loop system. This is the first randomized trial to investigate efficacy of this integrated system as compared to multiple daily injection therapy with SMBG.

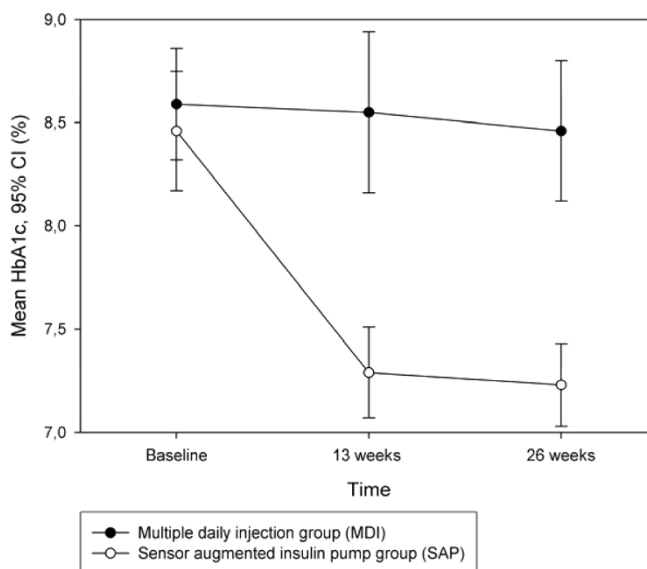
**Materials and methods:** In an investigator-initiated multinational multicenter controlled trial (Eurythmics trial ISRCTN22472013), we randomized 83 diabetes type 1 patients, age 18-65 years and HbA1c ≥ 8.2%, to receive either 26 weeks of continuous treatment with a sensor augmented insulin pump (SAP) (Paradigm REAL-Time) or standard care with multiple daily injection therapy (MDI). In both arms, treatment was preceded by 6 days of retrospective CGM use and treatment was optimized based on this information. A blinded six day CGM recording was taken in the MDI group at 13 and 26 weeks. HbA1c at 13 and 26 weeks was measured and the occurrence of severe hypoglycaemia (requiring third party assistance) was scored. Analyses were performed using ANCOVA models, adjusting for baseline values and centre.

**Results:** Baseline characteristics in the SAP group (n=44) and MDI group (n=39) were: mean age (± SD) 39 ± 12 and 37 ± 11 years; diabetes duration 17 ± 11 and 21 ± 9 years and 50% and 46% female, respectively, while 43/44 (98%) and 35/39 (90%) patients completed the trial. Mean HbA1c (± SD) in the SAP group decreased from 8.46 ± 0.95% to 7.23 ± 0.65% after 26 weeks. In the MDI group mean HbA1c was 8.59 ± 0.82% at baseline and 8.46 ± 1.04% after 26 weeks.

The mean difference in HbA1c change after 26 weeks was -1.10% (95% CI -1.41 to -0.71, P<0.001) in favour of the SAP group (Figure). The proportion of patients reaching EASD/ADA HbA1c target of <7.0% was 34.1% in the SAP group and 0.0% in the MDI group, P<0.001. Neither the difference in number of severe hypoglycemia episodes (4 in the SAP group versus 1 in the MDI group, P=0.22) nor the difference in change in sensor mean area under the curve (AUC) for hypoglycaemia (<72 mg/dl) (-0.20 mg/dl\*min 95% CI -0.52 to 0.11, P=0.20) was statistically significant.

**Conclusion:** Sensor augmented pump therapy effectively lowers HbA1c in poorly regulated type 1 diabetes patients without increase in hypoglycaemia. The magnitude of the difference in HbA1c change of -1.10% suggests an additive and possibly synergistic effect of the insulin pump, mealtime insulin dose advisor and CGM.

**Mean HbA1c values Eurythmics trial**



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