Sensor-augmented Pump Versus Multiple Daily Injections With Degludec as Basal Insulin for Insulin Therapy in Type 1 Diabetes

NCT03557892

Study protocol 21-JAN-2016

Study aim

The trial is aimed at verifying the superiority of a sensor-augmented pump (SAP) system, in comparison with optimized multiple daily injections (MDI) of insulin, using degludec as basal insulin, with respect to glycemic control, incidence of severe hypoglycemia, body weight, local reactions, treatment satisfaction, and patient preferences.

Study endpoints

The **primary endpoint** is the superiority of SAP versus MDI on HbA1c.

Secondary endpoints include:

1) Severe hypoglycemia
2) Change in body weight
3) Local reactions on the site of insulin administration and/or monitoring of glucose
4) Treatment satistfaction, measured using the Italian validated version of the WHO Diabetes Treatment Satisfaction Questionnaire.
5) Patients' preference for either treatment

Study design

The study is designed as a single-center, open-label, cross-over randomized trial.

Lo studio è disegnato come un trial randomizzato in cross-over, in aperto.

After verification of inclusion and exclusion criteria, enrolled patients will be randomized (using a computer-generated random number sequence) 1:1 to either SAP or MDI for 4 months, and then switched to the alternative treatment.

Treatments

- **MDI**: multiple daily injections of insulin, using degludec as basal insulin and lipsro, aspart r glulisine as prandial insulin. Dose adjustments will be performed on the basis of self-monitoring of capillary blood glucose (standard of care).
- **SAP**: Sensor augmented pump Vibe Animas Platinum integrated with glucose sensor Dexcom G4. Patients will be educated to manage glucose excursions detected by the sensor, and instructed to download sensor and pump data before each planned visit.

Duration of the study

- *Duration of enrolment*: 18 months
- *Duration of treatment*: 4 months for each treatment phase, with no wash-out.

Study population

Setting: Outpatients with type 1 diabetes referring to the Diabetes Clinic of SODc Diabetologia, AOU-Careggi, padiglione 28C, via delle Oblate 4, Firenze.

Inclusion criteria

1. Written informed consent
2. Diagnosis of type 1 diabetes, with a duration of diabetes of at least 2 years
3. Age 18-75 years
4. Current treatment with basal-bolus insulin, using a fast acting analog (lispro, aspart, glulisine) as prandial insulin and a long-acting analog (glargine , detemir o degludec) as basal insulin.
5. HbA1c< 8.0% (64 mmol/mol)
6. No severe diabetic complications (blindness for diabetic retinopathy, severe renal failure, lower extremity amputations)
7. Reported frequency of self-monitoring of blood glucose of at least 4 daily, with a meter allowing the download of data in electronic format

Exclusion criteria

1. HbA1c> 8.0% (64 mmol/mol)
2. Duration of diabetes>2 years
3. Uncompensated mental disorders
4. Pregnancy or lactation, or planned pregrancy within six months of enrolment
5. Any condition with a life expectancy <1 year

Insulin therapy and concurrent treatments

Concurrent treatments will be recorded at enrolment and their variations (if any) during the study will be collected. Patients will be asked to maintain the same formulations of insulin used at enrolment, with dose adjustments whenever needed for maintaining an adequate glycemic control.

Statistical plan

Determination of sample size.

The sample will be composed of 27 patients. This will allow to reach a 80% power of detecting ($p<0.05$) a difference in HbA1c between groups >0.5%, assuming a standard deviation of 0.83%.

Principal analysis (superiority): Variations of HbA1c in the two study phases will be compared using Student's paired t tests, which will also be used to compare end-of-treatment and baseline HbA1c for each treatment phase. A repeated measure linear regression model will be applied to compare the effects of the two treatments adjusting for treatment sequence. These analyses will be performed both by intention to treat (primary analysis), i.e. including all randomized patients and imputing missing data (if any) with the last observation carried forward (LOCF) method, and by protocol, i.e. restricted to patients actually using planned treatments.

Secondary endpoints: the same methods will be applied for analyses of secondary endpoints.