Prognostic value of Continuous Glucose Monitoring metrics for microvascular and macrovascular complications in diabetes using Freestyle Libre® system records and SNDS French claims database linkage (FACULTY)

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Study Planned

Administrative details

PURI

https://redirect.ema.europa.eu/resource/1000000188

EU PAS number

EUPAS1000000188

Study ID

1000000188

DARWIN EU® study

No

Study countries

☐ France

Study description

The FreeStyle Libre® (FSL) system is a glucose monitoring system that continuously measures glucose levels in the interstitial fluid of adults and children with type 1 (T1DM) or type 2 (T2DM) diabetes. In addition to the FSL system, LibreView (LV) is a secured platform storing glucose data and allowing the generation of individualized glucose report completing the glycemic picture [e.g., Time In Range (TIR), Glucose Variability and Hypoglycemic Exposure…]. In France, LV was part of the telemedicine program ETAPES (Expérimentations de Télémédecine pour l'Amélioration des Parcours En Santé) defined in Article 54 of the Social Security Financing Act for 2018 since May 2019 to experiment and assess the impact of telemonitoring for individuals with insulin treated diabetes. The application for registration was performed by the attending physician or by the physician who carries out the telemonitoring.

TIR or time in tight range (TITR) are potential alternatives to glycated hemoglobin (HbA1c), which is currently accepted as the gold-standard surrogate endpoint for diabetes clinical studies and management. A key step is now to understand if those new glucose metrics (e.g., TIR, TITR, GV and time in hypoglycaemia…) are linked to and can predict micro and macrovascular complications.

This study, to be performed using the SNDS (Système national des Données de Santé) French claims database, will assess firstly the relevance of the above diabetes monitoring metrics from CGMas predictors of micro and macrovascular complications, and secondly will investigate the added value of the ETAPES program to LV.

The objectives are to assess the prognostic value of CGM-derived diabetes monitoring metrics in determining the risk of microvascular and macrovascular complications, and to assess the clinical and economic benefits of the telemedicine program ETAPES for individuals using the LibreView diabetes telemonitoring platform with Freestyle Libre system.

Study status

Planned

Research institutions and networks

Institutions

Bordeaux PharmacoEpi, University of Bordeaux

France

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Institution | Educational Institution | Hospital/Clinic/Other health care facility | Not-for-profit | ENCePP partner

Contact details

Study institution contact

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Primary lead investigator

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Primary lead investigator

Study timelines

Date when funding contract was signed
Actual: 24/04/2022

Study start date
Planned: 31/03/2023

Data analysis start date
Planned: 30/06/2023

Date of interim report, if expected
Planned: 31/12/2024

Date of final study report
Planned: 30/09/2025

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Abbott

Regulatory

Was the study required by a regulatory body?

No

Is the study required by a Risk Management Plan (RMP)?

Not applicable

Methodological aspects

Study type

Study type list

Study topic:

Medical device

Study type:

Non-interventional study

Scope of the study:

Healthcare resource utilisation

Validation of study variables (exposure outcome covariate)

Data collection methods:

Secondary use of data

Study design:

Two cohort studies of subjects with diabetes: one from the LV system with SNDS data linkage (LV cohort), and a 2nd in the SNDS (cohort TM) including

those with diabetes with reimbursement for FSL (i.e., including subjects in and outside the LV cohort).

Main study objective:

The research questions are (i) to assess the relevance of CGM-derived diabetes monitoring metrics for the prediction of micro and macrovascular complications, (ii) to assess the added value of the ETAPES program to LV system.

Objective 1 - allowing to answer the research question (i) - is to assess the prognostic value of CGM-derived diabetes monitoring metrics for determining the risk of microvascular and macrovascular complications.

Objective 2 - allowing to answer the research question (ii) - is to assess the clinical and economic benefits of the telemedicine program ETAPES for individuals using the LibreView diabetes telemonitoring platform with Freestyle Libre system.

LV system was part of telemedicine that facilitates monitoring individual’s metrics, thus the ETAPES (Expérimentations de Télémédecine pour l’Amélioration des Parcours En Santé) program defined in Article 54 of the Social Security Financing Act for the year 2018 (https://solidarites-sante.gouv.fr/soins-et- Maladies/prises-en-charge-specialisees/telesante-pour-l-access-for-all-to-remote-care/article/telemonitoring-steps?) has been set up by French authorities since June 2019 to experiment and assess the telemonitoring for individuals with diabetes. The experiments concern five pathologies including diabetes. The application for registration is performed by the attending physician or by the physician who carries out the telemonitoring. The program allows us to evaluate the coherence and relevance of telemonitoring projects and aims to support healthcare professional and better meet health care needs. The telemedicine has an important role in the management, by improving access to care, reinforcing preventive actions and avoiding hospitalizations.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Name of medicine, other

FreeStyle Libre and LibreView (LV)

Medical condition to be studied

Diabetes mellitus

Population studied

Short description of the study population

Inclusion criteria

LV cohort: all adults from the LV system linked to the SNDS with a diagnosis of diabetes (T1DM or T2DM) and using FSL device for the first time since January 1st 2018.

TM cohort: all adults with diabetes identified in the SNDS database with a reimbursement for FSL, between 2018 and 2022. Within this cohort, individuals enrolled in the ETAPES program will be identified to compare: FSL users enrolled in ETAPES program versus FSL users not enrolled in ETAPES program.

Exclusion criteria

Individuals with discontinuous measurements of CGM will be excluded. The minimum number of consecutive days with CGM measurements that is required for each individual (for instance, 14 days every 90 days, as advised by the 2019 consensus) will be defined after discussion with the Scientific Committee and in view of the distribution of the CGM measurements over time.

Age groups

Adult and elderly population (≥18 years)

Adults (18 to < 65 years)

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Elderly (≥ 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

Estimated number of subjects

70

Study design details

Setting

To meet the objective 1, a cohort study of individuals with diabetes from the LV system with SNDS data linkage (LV cohort) will be carried out. It will include all individuals using FSL for the first time between 2018 and 2022 with a first date of glucose measure identified in LV system since 01/01/2018 (i.e., index date). Individuals of the cohort will have a 5-year history period before index date, and 1 to 6 years of follow-up in the SNDS. To cover the overall study period, LV data will be extracted from January 1st 2018 to December 31st 2022 in two steps: the first will be in 2024 and the second in 2025.

To meet the objective 2, a cohort study of individuals with diabetes with a reimbursement for FSL - including individuals who could not have been linked to SNDS and thus who are not present in the LV cohort -, between 2018 and 2022, will be carried out in the SNDS (cohort TM). Individuals of the cohort will have a 5-year history period before the provision date of the telemonitoring device and

from 1 to 6 years of follow-up. Within this cohort, individuals enrolled in the ETAPES Program will be identified to compare FSL users enrolled in ETAPES program versus FSL users not enrolled in ETAPES program.

Comparators

In the LV cohort, there is no comparative group.
In the TM cohort, the exposure will be the use of FSL (LPP codes: 1190296, 1102257, 1110720, 1103570) and the enrolment in ETAPES program allowing to define the following comparative groups: FSL users included in ETAPES vs. FSL users not included in ETAPES.

Outcomes

Primary outcome: In both LV and TM cohorts, the first occurrence of a microvascular complication (diabetic neuropathy, retinopathy or nephropathy) or a macrovascular complication [heart failure, MI, stroke, Peripheral artery disease (PAD)], considered as a composite outcome or separately.
Secondary outcomes:
In both LV and TM cohorts: all-cause mortality, hospital admission for any cause
In the TM cohort only: other healthcare resources use (medical visit, emergency visit, etc.), costs (from a payer perspective).

Data analysis plan

LV cohort:
−Description of baseline characteristics, the values and changes in CGM metrics during the follow-up period for individuals in the LV cohort, both overall and stratified according to absence/presence of any micro-macrovascular complications before the index date;
−Estimation of crude incidence rates for all outcomes, as well as cumulative incidence, using 1-Kaplan-Meier estimator (for death) and cumulative incidence function (CIF) for non-fatal outcomes, considering death as competing risk;

−Assessment of the prognostic value of each CGM metric for the different outcomes using DRS-adjusted Cox model in both LV sub-cohorts, with and without prior micro-macrovascular complications. In these models, the independent variables include DRS (in deciles), CGM metrics calculated within the initial 90-day time window, and exposure to cardiovascular drugs during the follow-up period as time-varying covariates. Sensitivity analyses will also be conducted using alternative time windows (14 days, 1 month, 6 months and 12 months) for CGM metrics calculation.
−Comparison of the prognostic value of different CGM metrics using measures such as concordance index (c-index), time-dependent AUC, integrated Brier score…;
−Assessment of the association between each CGM metric and the primary outcomes using a “nested case-control design”;

TM cohort:
−Description of baseline characteristics of the TM cohort overall and according to enrollment in the ETAPES program or not (FSL users with ETAPES versus FSL users without ETAPES);
−Comparison of the risk of clinical outcomes between TM sub-cohorts using IPTW-adjusted Cox model for death and IPTW-adjusted Fine and Gray model for non-fatal outcomes.
−Comparison of reimbursed costs between TM sub-cohorts using an IPTW-adjusted multivariable linear regression model and of the healthcare resource utilization during the follow-up period using standardized differences.

Data management

Data sources

Data source(s)

Système National des Données de Santé (French national health system main database)

Data source(s), other

Plateforme LibreView, France

Data sources (types)

Administrative healthcare records (e.g., claims)

Other

Data sources (types), other

LibreView (LV) is a secured platform storing glucose data and allowing the generation of individualized glucose report completing the glycemic picture. LV allows physicians and their individuals to download, view and analyze data from the FSL reader, the FreeStyle LibreLink application, the FreeStyle Libre Pro and other FreeStyle readers.

Use of a Common Data Model (CDM)

CDM mapping

No

Data quality specifications

Check conformance

Yes

Check completeness

Yes

Check stability

Yes

Check logical consistency

Yes

Data characterisation

Data characterisation conducted

Not applicable