AVENIR project:: AGE in Vascular risk Estimation and Normalisation by Intensified Reduction in diabetes type 2

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Observational non invasive

Summary

ID

NL-OMON34555

Source
ToetsingOnline

Brief title
AVENIR

Condition

- Diabetic complications

Synonym
diabetic cardiovascular complications

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Sanofi-aventis,unrestricted;investigational grant SanofiAventis

Intervention

Keyword: cardiovascular, complications, diabetes, skin autofluorescence

Outcome measures

Primary outcome

The difference in reduction from baseline to the end of the study (one year) in systolic blood pressure and in blood pressure, lipid lowering and anitdiabetic medication between the two arms. Systolic blood pressure has been used for power analysis.

Secondary outcome

-changes over 1 year in HbA1c, LDL-cholesterol; idem for autofluorescence (AGE reader), UKPDS risk score between baseline and one year.

- changes in UKPDS score and SAF from baseline to 1 year, compared between the subgroups within the SAF+UKPDS arm, in which CV risk estimated with SAF and that estimated with the UKPDS risk engine is in a higher or lower risk class than that estimated with the UKPDS risk score, compared to the group in whom both risk class estimates are concordant.

-differences between the abovementioned concordant and discordant subgroups in target treatment values of blood pressure and lipids used by the treating physician. This will be assessed using a questionnaire

-questions about the effect of the availability of skin autofluorescence and of the UKPDS RE values on treatment as perceived by the treating physician using a questionnaire

In addition the reduction from baseline to one year in systolic blood pressure,

and in blood pressure, lipid lowering and anitdiabetic medication, and in lipid and HbA1c levels will also be compared in an aselected (only age decade and sex disitribution matched) sample of T2DM patients from the same center in whom neither SAF nor UKPDS score has been measured or provided to the treating physician. To avoid potential study participation bias, we propose not to ask for patient consent. The selection wil be made once the general characterisitcs (age and sex distribution) of the randomised patiens are known, so after the 1st inclusion year. Otherwise, similar end point data will be collected as in the randomised participants, except those of the UKPDS score and SAF measurements. The (local) investigators will select these patients from their hospital database, and will regsiter the data in an anonimised manner.

Study description

Background summary

The UKPDS study showed that good glycemic control in patients with type 2 diabetes mellitus (DMT2) results in a significant reduction in microvascular complications. A long-term follow-up extension of the study revealed that early intervention and good glycemic control early in the disease process, will result in a long-term reduction in cardiovascular (CV) complications. A recent study in The Netherlands showed in line with siilar observations in Scotland and the US that the mortality risk of patients with DMT2 that were relatively well controlled (HbA1c =7%) and treated (>=30% on statins and RAS inhibitors) has become comparable to that of the general population (Lutgers 2009).These results show that a normal life expectancy is achievable in patients with DMT2 when adequately controlled and treated. Good CV risk estimation is essential to guide such treatment.
The UKPDS risk engine is specifically developed to assess the morbidity and mortality risk in patients with DMT2 (Stevens 2001). However, in general and hospital practice this risk engine is still relatively little used , partly because of the large (10) number of parameters that have to be measured and filled-in, and because of the known limitations of the risk engine as a predictor. This emphasizes the importance of additional or alternative risk

factors that can be used to monitor the CV risk and to adjust or intensify treatment.
Skin auto fluorescence (SAF) was recently introduced as an alternative tool for cardiovascular risk assessment in diabetic patients (Meerwaldt 2007; Lutgers 2009). In more than 20% of patients with DMT2 the addition of SAF to the UKPDS risk score leads to reclassification of *low* or *medium* risk patients to *high* risk patients, or visa versa. Preliminary results of the AURORA study in the Netherlands reveal that SAF has a high correlation with the presence of CV complications. The non-invasive nature of the SAF measurement makes this a potential valuable and important contribution to the currently available risk engines, especially for those patients without concurrent CV complications.

Study objective

The aim of this randomised, parallel study in patients with DMT2 is to investigate if the added use of skin autofluorescence to the UKPDS risk score will lead to changes in systolic blood pressure and medical treatment (primary measures of effect) compared to *standard* CV risk classification using the UKPDS risk engine,.

Study design

The objective will be tested in a randomised, controlled two-arm implementation study, in appr. 930 patients with type II diabetes without known cardiovascular disease, treated by hospital-based physicians in internal medicine. T2DM patients will be randomised to the first arm in which the physician receives both the UKPDS RS, and the SAF measurment result, or to the second arm in which the physician only receives the UKPDS RS result. Changes in treatment policy between baseline and one year will be assessed. For this purpose, changes in systolic blood pressure and in medical treatment between baseline and 1 year follow-up (primary end points), and the changes in lipids and glycemic contro/HbA1c (secondary end points) will be assessed.

Within the SAF+UKPFDS arm, measures like net reclassification will also be calculated.in subgroups with concordant and discordant results of SAF and UKPDS RS.
As stated above a concordance/discordance analysis within the participants randomised to the arm with provision of both UKPDS RE and SAF resutlts will be performed by a form of reclassification analysis, classifying four groups:
oGroup 1 (*high/low group*), where risk classification at baseline using the UKPDS risk engine is different from risk classification using an AGE Reader: i.e. patients classified as UKPDS risk score > 10% but autofluorescence < median.
oGroup 2 (*low/high group*), where risk classification at baseline using the UKPDS risk engine is different from risk classification using an AGE Reader:

i.e. patients classified as UKPDS risk score < 10% but autofluorescence > median.
oGroup 3 (*high/high group*), where risk classification at baseline using the UKPDS risk engine is similar to risk classification using an AGE Reader: i.e. patients classified as UKPDS risk score > 10% and autofluorescence > median.
oGroup 4 (*low/low group*), where risk classification at baseline using the UKPDS risk engine is similar to risk classification using an AGE Reader: i.e. patients classified as UKPDS risk score < 10% and autofluorescence < median.

Study burden and risks

All measurements are also performed in regular clinical practice: the project involves a registry of performed laboratory follow-up assessments and treatment changes. It also involves the performance of SAF measurements at baseline and after one year. No extra visits, blood samples or physical examinations.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

type 2 diabetes mellitus

Exclusion criteria

factors which may affect UKPDS risk engine score or autofluorescence measurement, such as South Asian descent, diffuse skin dsease

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-05-2011
Enrollment:	930
Type:	Actual

Ethics review

Approved WMO

Date:	01-03-2011
Application type:	First submission

Review commission: METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL33505.042.10