AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA

FINISHED PRODUCT: None
ACTIVE INGREDIENT: None

Study No: D1843R00243; NCT02355145
REALITY: A NON-INTERVENTIONAL STUDY TO OBSERVE THE RATIONALE OF SELECTING ADD-ON THERAPY FOR TYPE 2 DIABETES INADEQUATELY CONTROLLED WITH METFORMIN IN REAL-LIFE PRACTICE AT 1 YEAR DISTANCE

Developmental Phase: Non-Interventional Study
Study Completion Date: 28/07/2016
Date of Report: 16/03/2017

Study type

This is a non-interventional, multicenter study to observe the main criteria used in clinical practice by physicians when selecting the second-line add-on therapy in patients with inadequately metformin-controlled type 2 diabetes in 2 time points at 1 year distance.

OBJECTIVES:

(a) Primary objective

The primary objective of this NIS is to describe and compare the main criteria used by physicians from regular outpatient setting in selecting the add-on therapy in patients with inadequately metformin-controlled type 2 diabetes in 2 time points at 1 year distance by assessment of patient, and/or agent characteristics and/or physician decision. The Investigators will be provided with a list of reasons for each category (see Appendix B), indicating which category was considered the most relevant in selecting a specific add-on class for each patient.

(b) Main secondary objectives

1. To describe the usage of add-on therapies in type 2 diabets and changes observed in 1 year by evaluation of the classes of the drugs used and duration of treatment.

2. To evaluate the prevalence of comorbidities and diabetes complications in study groups.

3. To evaluate the percentage if patients with target HbA1c level < 7% at the 2 time-points, by assessment of their last available HbA1c value.

4. To describe the characteristics of the disease at the time of initiating the add-on therapy in Bulgarian patients with type 2 diabetes by evaluating the year of type 2 diabetes duration and the year of starting the add-on therapies.

METHODS:

This was a non-interventional, multicentre study to observe the main criteria used in clinical practice by physicians when selecting the second-line add-on therapy in patients with inadequately metformin-controlled type 2 diabetes in 2 time points at 1 year distance.

The assignment of the patients to a particular add-on therapy was not decided in advance by the NIS protocol, but fell within current practice and the prescription of medicine was clearly separated from the decision to include the subject in the study. No additional diagnostic and monitoring procedures were applied to patients, other than daily clinical practice and epidemiological methods were used for the analysis of collected data. The intention of the study was to collect data on patients with type 2 diabetes and oral add-on therapies under routine clinical care.

The patients participated in only one study visit, at the time of enrolment, when they provided the written informed consent, allowing the access to their data. Data were collected by reviewing the medical records of patients.

The study was completed between April, 2015 (First Patient First Visit was on 02 April 2015) and July, 2016 (Last Patient Last Visit was on 28 July 2016).

Target subject population

Target population was represented by patients with type 2 diabetes inadequately controlled with metformin therapy receiving any add-on antidiabetes treatment.

Diagnosis and Main Criteria for Inclusion:

Inclusion Criteria

1. Provision of subject informed consent
2. Female and/or male aged 18 years and over
3. Diagnosis of type 2 diabetes mellitus
4. Patients considered inadequately controlled with metformin with a current treatment based on any add-on diabetes therapy

Exclusion criteria:

1. Diagnosis of type 1 diabetes
2. Current antidiabetes treatment with oral monotherapy
3. Insulin treatment for type 2 diabetes
4. Current participation in any clinical trial

5. Patient who have been enrolled in the study at point 1 can not be enrolled at point 2

Evaluations:

Primary endpoint

Primary endpoint was calculated on the Per-Protocol Population, that is on the set of all enrolled and eligible subjects with no missing primary variable data.

Secondary endpoints

Secondary endpoints were calculated on the Full Analysis Set, that is on the set of all enrolled and eligible subjects.

Statistical Methods:
Primary variable
The primary objective of this NIS was to describe and compare the main criteria used by physicians (regular outpatient setting) in selecting the oral add-on therapy in patients with inadequately metformin-controlled type 2 diabetes in 2 time points at 1 year distance.

Secondary variables
• To describe the usage of oral add-on therapies in type 2 diabetes and changes observed in 1 year.
• To evaluate the prevalence of comorbidities and diabetes complications in study groups.
• To evaluate the percentage of patients with target HbA1c level < 7% at the 2 time-points.
• To describe the characteristics of the disease at the time of the initiating the oral add-on therapy in Bulgarian patients with type 2 diabetes.

RESULTS:

Primary endpoint:

Three categories were investigated as potential explanation of decisions made during selection of add-on therapies.

After the baseline and the repeated data collection it can be declared that ‘Patient characteristics’ were and remained the most important category in selection of the therapies, even with a slightly increasing importance (overall 55.2%, 52.0% and 58.4% at Moment 1 and Moment 2).

Category ‘Agent characteristics’ is the second most important factor in the overall sample (24.0%), but only at Moment 2 (25.0%), while it was only the 3rd in the rank at Moment 1 (23.0%).

Category ‘Physician decision’ is the 3rd most important factor in the overall sample (20.8%), and at Moment 2 (16.6%), but it was the 2nd most important factor at Moment 1 (25.0%).

The changes with the original observations are summarised in (Table 21). The table clearly shows that only the importance of ‘Patient characteristics’ increased (6.4%), while both ‘Agent characteristics’ and ‘Physician decision’ decreased (-2.9% and -7.9% respectively).

The highest increase was observed in the sub-categories 'Overweight' (6,4%), 'Risk of inducing hypoglycemia' (6.0%) and 'Effect on weight' (5.7%).

Secondary endpoints:

- Usage of add-on therapies

The mean time between diagnosis of Type 2 diabetes 7.7 (Moment 2) and 8.2 (Moment 1) year with a median of 6.8 and 7.2 year respectively. This factor can be considered identical in the two samples.

Great majority of the patients (99.2% and 99.6%) were treated with metformin. The mean duration of that treatment was 3.8 (SD: 4.0) year at Moment 1 and 5.6 (SD:5.0) at Moment 2. Though it is a remarkable difference, as the second sample followed the first sample only with one year, this difference can rather be a consequence of sampling technics, maybe geographical differences.

The duration of the first add-on therapy was 2.7 (SD: 3.4) year (Moment 1) and 0.8 (SD: 1.5) year at Moment 2. This big difference cannot be explained with other (e.g. demographic) data of the study. Similarly, even with a relatively high sample sizes, sulfonylureas were applied for 3.8 year as average at Moment 1 (n: 218, SD: 4.1 year) while it was only 1.3 year at Moment 2 (n: 180, SD: 2.1). Similar effect can be stated for DDP-4 inhibitors: the mean duration was 1.4 year (n: 136, SD: 1.6) vs 0.5 year (n: 151, SD: 0.8) at Moment 1 and 2 respectively.

Great majority of the patients mentioned of the application of only 1 add-on therapy (74.0% and 77.4%) and only 4-5% of the patients mentioned more than 3-4 add-on therapies.

There are data for time between 1st and 2nd add-on therapies only for 35 and 17 patients at Moment 1 and Moment 2 respectively. This small number of data does not provide reliable statistics.

- Prevalence of comorbidities and diabetes complications

Six hundred and twenty subjects (61.7% of the total 1005 patients) suffered from any diabetes complications in the pooled sample. At Moment 1 64.8% of the 500 patients had diabetes complications, which decreased to 58.6% for Moment 2.

According to therapeutic areas neuropathy complications were the most frequent in both samples, 49.8% and 42.2% in Moment 1 and 2 respectively. The observed decrease cannot be considered statistically significant.

Cardiovascular complications were also common, especially at Moment 1. The originally observed 33.4% decreased to 25.5%, which is a statistically significant difference ($p = 0.006$).

Although Nephropathy was observed only in 3.4% (pooled sample), but the baseline 2.8% increased to 4.0% which was a statistically significant increase.

Retinopathy (overall 4.0%), Foot damage (overall 0.9%), Osteoporosis (overall 1.6%) and 'Other' (overall 7.3%) did not show a statistically significant change between Moment 2 and Moment 1.

- Percentage of patients with target HbA1c level < 7%

The mean HbA1c level was statistically significantly higher at Moment 2 than at Moment 1 (7.5% (SD: 1.36%) vs 7.8% (SD: 1.53%), p = 0.039).

While 37.6% of the patients were under 7% at Moment 1, this ratio decreased to 31.7% by Moment 2. This is the main reason of the statistically significant increase of the mean, because the HbA1c distributions were very similar in the other categories.

- The characteristics of the disease at the time of initiating the add-on therapy

All the relevant information can be found in the previous sections. Demographic and baseline characteristics are summarized in Section 11.2. Prevalence of comorbidities and diabetes complications are tabulated in Section 11.4.2. The HbA1c levels statistical characteristics are analysed in Section 11.4.3. Finally, the time from diagnosis, the duration of metformin treatment, time between the metformin treatment and 1st add-on therapy, the number of add-on therapies and the duration between the 1st and 2nd add-on therapies can be found in Section 11.4.4.