AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable.
ACTIVE INGREDIENT: Not applicable.

Study No: NIS-CME-XXX-2012/1-RO

OPTIMISE - CEEMEA - OPtimal Type 2 dIabetes Management Including benchmarking and Standard treatment in CEEMEA

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Developmental Phase: No

Study Completion Date: **31/03/2014**

Date of Report: 12 **november 2014**

OBJECTIVES:

Primary

· To investigate whether the use of benchmarking could improve quality of patient care, in particular the control of diabetes, lipids, and blood pressure, expressed as the percentage of patients in the benchmarking group achieving pre-set targets for hemoglobin A_{1c} (HbA_{1c}), low-density lipoprotein-cholesterol (LDL-C), and systolic blood pressure (SBP) versus (vs.) control group (non-benchmarking group) after 12 months of follow up.

Secondary:

· To investigate whether the use of benchmarking could improve quality of patient care, in particular the control of diabetes, lipids, and blood pressure, expressed as the percentage of patients achieving pre-set targets for HbA_{1c}, glycaemia, LDL-C, and SBP values after 12 months of follow up vs. baseline.

· To investigate whether the use of benchmarking could improve quality of patient care, in particular the control of diabetes, lipids and blood pressure, expressed as the percentage improvement in HbA_{1c}, glycaemia, lipidogram, and blood pressure values after 12 months of follow-up versus baseline.

· To follow up on markers of preventive screening; retinopathy, neuropathy, dietary counseling, smoking habits, body mass index (BMI), waist circumference, physical activity.

· To evaluate the LDL-C parameter of the primary and secondary objectives according

to Adult Treatment Panel III (ATP III) guidelines.

METHODS:

This was a multinational, multi-centre, observational, prospective study that included 734 patients diagnosed with diabetes type 2, treated or untreated, insulin dependent or not insulin dependent.

Physicians were randomised 2
to 1 by a centralised randomisation procedure into 1 of 2 groups in the study: (1) a group of physicians receiving feedback on the level of control of cardiovascular risk factors for their patients as well as central benchmarking information (comparing their performance with the performance of other investigators in an anonymous way), and (2) another group receiving feedback on the risk factors of their patients only. It was planned that each of the sites would recruit 20-25 patients.
Formal comparison testing between benchmarking vs. control groups although considered exploratory was performed for each of the primary endpoints via a logistic regression model with factors for group and country of recruitment (Romania and Bulgaria) and baseline value as a continuous covariate with site fitted as a random effect.

Target Patient Population

Patients diagnosed with type 2 diabetes, treated or untreated, insulin dependent or not insulin dependent, were included in this study.

Inclusion Criteria

Patients had to fulfill all of the following criteria to participate in the study:
1. Provided patient informed consent
2. Female or male aged 18 years and over
3. Patients diagnosed with type 2 diabetes, treated or untreated, insulin dependent or not insulin dependent
4. Able to read and send a message through Short Message Service (SMS) (if SMS applicable)

The prescription of the medicinal product was clearly separated from the decision to include the patient in the NIS.

Exclusion Criteria

Patients could not participate in the study if they had any of the following exclusion criteria:
1. Type 1 diabetes mellitus
2. Gestational diabetes mellitus
3. Hospitalisation at the moment of enrollment in the study
4. Participation in any clinical study.

RESULTS:

Primary Analysis:

The percentage of patients who reached the HbA_{1c} target (ie, $HbA_{1c} \leq 7\%$) at 12 months follow up was 69.9% in the control group and 54.7% in the benchmarking group. The difference between groups in the patients who reached the HbA_{1c} target was not

statistically significant (95% confidence interval [CI]: -33.5, 3.0). A logistic regression analysis was also carried out, adjusting for the covariates baseline HbA_{1c}, site, and country. The corresponding odds ratio was 0.43, with a 95% CI of 0.20, 0.93.
The percentage of patients who reached the LDL-C target, (ie, LDL-C ≤70 mg/dL) according to European Society of Cardiology (ESC) guidelines, at 12 months follow up was 14.8% in the control group and 15.9% in the benchmarking group. In the logistic regression analysis, adjusting for covariates baseline LDL-C, site, and country, patients in the benchmarking group were just as likely to reach the LDL-C target, than those in the control group (odds ratio: 0.98 and 95% CI: 0.46, 2.07). Furthermore, no statistically significant difference (95% CI: -8.9, 11.1) was found in patients reaching the LDL-C target between the control and benchmarking groups. .
The percentage of patients who reached the SBP target of ≤130 mm Hg at 12 months follow up was 64.0% in the control group and 60.9% in the benchmarking group. The odds ratio from the logistic regression analysis, adjusted for baseline covariates SBP, site, and country, was not significant (odds ratio: 0.93, 95% CI: 0.44, 1.94).

Secondary Analyses:
For HbA_{1c}, a greater percentage of patients in the control group (12.9%) compared with the benchmarking group (5.8%) had shifts from too high HbA_{1c} at baseline to good HbA_{1c} at month 12. Using last observation carried forward (LOCF) methodology, at the last observation, a greater percentage of patients had shifts from too high HbA_{1c} at baseline to good HbA_{1c} at LOCF in the control group (13.3%) compared with the benchmarking group (6.5%). At month 4 and 8, the control group compared with the benchmarking group showed increased percentages of patients with too high HbA_{1c}.
For glycaemia, shifts at month 12 and the last observation (using LOCF methodology) were similar in the control and benchmarking groups. At month 4, greater percentages of patients in the control group (58.3%) compared with the benchmarking group (52.2%) shifted from baseline categories (normal, borderline, or diabetes) to diabetes. At month 8, greater percentages of patients in the control group (16.7%) compared with the benchmarking group (9.7%) shifted from diabetes to borderline glycaemia. At months 4, 8, 12, and the last observation (using LOCF methodology), decreases from baseline in glycaemia were greater in the benchmarking group compared with the control group. No pattern was found between the control and benchmarking groups for percent changes across the months.
The percentage of patients who reached the glycaemia target (<110 mg/dL) at 12 months follow up was 14.9% in the control group and 17.6% in the benchmarking group. No statistically significant differences were found between groups in the logistic regression analysis (odds ratio: 0.91, 95% CI: 0.34, 2.46) or in the differences between proportions (95% CI: -10.5, 16.0).
For LDL-C (ESC Guidelines), shifts at month 12 were similar in the control and benchmarking groups. At month 4, 8, and the last observation (using LOCF methodology), shifts from baseline categories (good, borderline, or too high) to too high LDL-C were greater in the control group compared with the benchmarking group. At month 4, in the benchmarking group, the total percentage of patients with shifts from 3 categories (good, borderline, or too high) at baseline to good LDL-C increased from month 4 (11.4%) to month 8 (17.9%), and to LOCF (16.6%). This trend was not seen in the control group.

For LDL-C (ATP III Guidelines), results from the shift analyses were similar to the results using the ESC guidelines. The percentage of patients who reached the LDL-C target（≤100 mg/dL, according to ATP III guidelines) at 12 months follow up was 50.7% in the control group and 53.3% in the benchmarking group. In the logistic regression analysis, controlling for covariates baseline LDL-C, site, and country, no statistically significant differences were found between the groups in reaching the ATP III guideline-defined target for LDL-C (odds ratio: 0.98, CI: 0.49, 1.98)

Decreases from baseline and percent decreases from baseline in total cholesterol (TC) were seen at all visits in both control and benchmarking groups, but no consistent pattern was found between groups. In general, increases from baseline and percent increases from baseline in high-density lipoprotein cholesterol (HDL-C) were seen at visits in control and benchmarking groups, with greater increases found in the benchmarking group. At month 12, the percent change from baseline in HDL-C was 5.8% in the benchmarking group and 4.8% in the control group. In general, decreases from baseline in triglycerides (TG) were seen at visits in control and benchmarking groups, with greater decreases found in the benchmarking groups.

For SBP, shift analyses showed improvements in both groups. A greater percentage of patients in the benchmarking group (14.1%) compared with the control group (6.4%) had shifts from too high SBP at baseline to borderline SBP at month 12. Although at month 4, a greater percentage of patients shifted to too high SBP in the benchmarking group (14.6%) compared with the control group (7.8%), at other time points the shifts from baseline categories (too high, borderline, or good) to too high, borderline, or good were similar between the groups.

Markers of preventive screening: At the month 4 visit, a greater percentage of patients in the benchmarking group compared with patients in the control group had a foot examination performed within the past 12 months. The percentages of patients who had a foot examination in the past 12 months were similar between the control and benchmarking groups at month 8 (60.8% and 60.1%, respectively) and month 12 (52.5% and 51.6%, respectively).

Greater percentages of patients had an ophthalmological examination in the past 12 months in the benchmarking group compared with the control group at the month 4 (33.2% and 23.4%, respectively) and at the month 12 visit (35.2% and 26.0%, respectively). At the month 8 visit, a greater percentage of patients in the control group compared with patients in the benchmarking group had an ophthalmological examination performed within the past 12 months.

In general, decreases from baseline and percent decreases from baseline in waist circumference were seen at visits in both control and benchmarking groups, but no consistent pattern was found between groups. At month 12, percent change from baseline in waist circumference was -0.7% in the benchmarking group and -0.8% in the control group. Decreases from baseline and percent decreases from baseline in BMI were seen at all visits in both control and benchmarking groups, with greater decreases seen in the benchmarking group. At month 12, percent change from baseline in BMI was -1.5% in the benchmarking group and -0.7% in the control group.

At months 4, 6, 12, and the last observation (using LOCF methodology), the following was found: the control and benchmarking groups had similar percentages of smokers; the percentages of nonsmokers were greater in the control group compared with the benchmarking group; and the percentages of ex-smokers were greater in the benchmarking group (13.3%) compared with the control group (9.3%).

At months 4, 6, 12, and the last observation (using LOCF methodology), a greater percentage of patients in the benchmarking group compared with patients in the control group received dietary advice within the past 6 months. At month 12, the percentage of patients who received dietary advice within the past 6 months was 86.3% in the benchmarking group and 64.2% in the control group.
The percentage of patients with an improvement in physical activity was similar between the control and benchmarking groups at month 4 and 8; at month 12, a greater percentage of patients in the benchmarking group compared with the control group reported an improvement in physical activity. The number of steps decreased from baseline to month 4, 8, 12, and LOCF in control and benchmarking groups, and to a greater degree in the control group. At month 12, the change from baseline in number of steps was -27.4 in the benchmarking group and -62.6 in the control group. The results from the analysis of covariance (ANCOVA) at month 12 showed baseline steps ($p<0.001$) and country ($p<0.001$) were statistically significant. The adjusted mean difference in steps (-10.3) was not statistically significant between groups (95% CI: -94.5, 73.9).
At month 4, 8, 12, and the last observation (using LOCF methodology), similar percentages of patients in the control and benchmarking groups were receiving treatment for diabetes; and among the patients who were receiving treatment for diabetes, greater percentages in the control group compared with the benchmarking group were receiving insulin. At month 12, the percentage of patients receiving insulin was 18.0% in the benchmarking group and 24.5% in the control group. The mean dose of insulin was similar between control and benchmarking groups.
At month 4, 8, 12, and the last observation (using LOCF methodology), greater percentages of patients in the benchmarking group compared to the control group were receiving lipidlowering (at month 12, 74.3% and 62.3%, respectively), antihypertension (at month 12, 88.0% and 81.4%, respectively), and aspirin (acetylsalicylic acid) (at month 12, 55.7% and 41.2%, respectively) medication. At month 12, the percentage of patients taking lipid lowering medication was 74.3% in the benchmarking group and 62.3% in the control group.

Study Limitations

The sample size could have been a limitation in the current study. Probably a higher sample size could have allowed us to use a more appropriate statistical approach including more relevant variables in the statistical models (eg, disease severity, disease duration, treatment, comorbidities).