

STUDY REPORT SYNOPSIS

A non-interventional study on T2DM patient's characteristics and management by GPs and endocrinologists in the Russian population (THESEUS)

Milestones:	08.11.2018 final protocol version 4.0
Phase of development:	Non-interventional study (NIS)
Sponsor:	AstraZeneca

This study was performed in compliance with Good Clinical Practice (GCP) and Good Pharmacoepidemiology Practice (GPP), including the archiving of essential documents.

This submission/document contains trade secrets and confidential commercial information, disclosure of which is prohibited without providing advance notice to AstraZeneca (AZ) and opportunity to object.

Background/rationale:

Diabetes mellitus type 2 (T2DM) is a global and costly health care burden. For the latest decades, we can see the growing rate of T2DM. In Russian Federation the prevalence of T2DM was raised by 2.2 millions during the last 10 years. According to current international guidelines, management should be complex, and include not only HbA1c control, but also blood pressure control, lipid management and antiplatelet therapy. The management of T2DM remains suboptimal: about 60% of patients do not achieve glycemic targets, more than half of them have arterial hypertension and are overweight.¹⁻⁶

For the last 10 years, a lot of new classes of oral antidiabetic drugs (OAD), offering new benefits for patients were entered clinical practice, the most recent of them is sodium-dependent glucose cotransporter 2 (SGLT2) inhibitors. It possesses insulin-independent mechanism of action and effects on cardiovascular (CV) risk factors: reduce blood pressure and weight. In the latest European Guidelines on cardiovascular disease prevention it is suggested that in patients with T2DM and cardiovascular disease (CVD), the use of an SGLT2 inhibitor should be considered early in the course of the disease to reduce CV and total mortality (class A, level B).⁷⁻⁸

Current T2DM management approach is focused on glycemic control in the context of a comprehensive cardiovascular risk factor reduction program, thereby supporting a shift from specialized to primary care. However, a primary care model is not very well suited for chronic disease management, it is mainly focused on quick problem solving. It is known that management of diabetes is frequently suboptimal in primary care settings, where providers often fail to intensify therapy when glucose plasma levels are high, a problem named as clinical

inertia. According to data, in some countries more than 90% of T2DM patients are managed by general practitioners (GPs), who may not be always aware of up-to-date information and new treatment approaches in T2DM. In the same time, there are findings, suggesting that diabetes management can be successfully performed by GPs in structured framework.^{3,9-14}

In Russian Federation diabetes management in some regions can be provided by GPs in primary care. The most of T2DM patients are managed by endocrinologists. Currently, it is a lack of real-world data, describing T2DM patients and treatment approaches in primary care settings in Russian Federation. This study provided the first epidemiological data about patient characteristics and treatment approaches in primary care. This would be important in pinpointing avenues to manage these patients more effectively, especially given the availability of many new antidiabetic therapies, such as SGLT2 inhibitors.

Objectives:

Primary objective:

To describe demographic and clinical characteristics of T2DM patients managed by HCPs (either endocrinologists or general practitioners) (demographical, clinical and treatment characteristics) before dapagliflozin initiation:

- mean age;
- age distribution;
- gender distribution;
- mean duration of T2DM;
- HbA1c (mean and distribution)
- Weight (mean)
- SBP (mean and distribution)
- DBP (mean and distribution)
- Proportion of T2DM patients with diabetic complications
- Proportion of patients with T2DM treatment intensification during 3 months before inclusion in the study
- Proportion of patients with different treatment regimen
- Proportion of patients on treatment with different classes of antidiabetic therapy
- Proportion of patients on different classes of concomitant therapy

Secondary objectives:

1. To describe mean reduction of HbA1c, SBP, DBP and weight at least 3 months after dapagliflozin initiation in patients enrolled in the study;
2. To describe proportion of patients with HbA1c <7.0% and SBP<140 mm Hg at least 3 months after dapagliflozin initiation and later in patients enrolled in the study
3. To describe proportion of patients with AEs during at least 3 months after dapagliflozin initiation and later in patients enrolled in the study.

Study design: multi-centre observational, ambispective study.

Data source: Data was collected from patient medical records.

Study population: Subjects with T2DM 18 years and older, who were managed by endocrinologists or GPs in 45 outpatient sites.

Inclusion criteria:

Male and female patients were eligible to participate if all the following criteria apply:

- 1) Age 18 and older;
- 2) Established diagnosis of T2DM (ICD-10 code E11.2-E11.9)
- 3) The current treatment with dapagliflozin prescribed at least 5 months before the date of patient's enrollment in the study;
- 4) Written voluntary informed consent has been provided
- 5) Management in outpatient setting.

Exclusion criteria:

- 1) Type 1 diabetes
- 2) Current participation in a clinical trial
- 3) Presence of any condition/circumstance which in the opinion of the investigator could significantly limit the follow up of the patient (e.g. tourist, non-native speaker or does not understand the local language, psychiatric disturbances).
- 4) Presence of serious/severe co-morbidities in the opinion of the investigator, which may limit treatment approach as usual.
- 5) Treatment with drugs affecting glucose homeostasis (e.g., systemic glucocorticosteroids) within 3 months before to the 1st Visit

Statistical methods: All statistical analysis was performed using the R[®] statistical software system. A comprehensive Statistical Analysis Plan was prepared before database lock. For statistical analysis of results of this non-interventional study descriptive statistics methods was used. No hypothesis was verified or refuted at that. Continuous variables were added up using descriptive statistics techniques (sample number, mean value, standard deviation, median, the 25th and 75th percentile, minimum and maximum). Categorical variables were added up using one-way tables (N, %). Additionally 95% confidence interval for the mean and proportion was also provided.

Results: There were enrolled 917 patients. The majority of patients were female (66.19%) and 55-65 years old (45.04%). The mean age was 58.07 (9.36) years.

The mean duration of T2DM was 79.69 (69.62) months.

The study results showed that before dapagliflozin initiation, only 7.80% of patients had a level of HbA1c <7% and 45.56% had a value of SBP <140 mm Hg.

After at least 3 months of treatment with dapagliflozin, the mean change of HbA1c, weight, SBP and DBP were as follows: -1.68 (1.27)%; 7.22 (6.55) kg; -8.54 (11.68) mm Hg; -5.93 (8.14) mm Hg correspondently. The proportion of patients with HbA1c <7% increased up to 44.38% and with SBP level <140 mm Hg increased up to 81.96%.

Most of the patients (57.58%) had diabetic microvascular complications in medical history, among them the most widespread was diabetic neuropathy (54.19%). In contrast, only 8.18% patients had diabetic macrovascular complications and in the most of cases it was some revascularization procedures (43.02%).

In total 12.76% patients had treatment intensification during 3 months before enrollment into the study. Usually, it was switch between OAD (52.99%, n=62/917).

The most common treatment regimen included two oral antidiabetic drugs (OAD) (35.44%), and the most commonly prescribed classes of antidiabetic therapy was monotherapy with a drug other than metformin (29.34%). No patients were prescribed metformin + iSGLT2 combination.

As it expected the most commonly prescribed concomitant therapy was antihypertensive medicine, in particular, RAAS inhibitors were prescribed in 51.58% patients. However, the statins as part of lipid management were prescribed only 23.01% patients.

Additional analysis revealed that the two most interdependent factors in terms of achieving target goals of therapy were HbA1c level <7% and SBP level <140 mm Hg.

Conclusion: This study provided the first epidemiological data regarding the patient characteristics and treatment approaches in primary care in Russia. It results showed that the management of T2DM patient remains suboptimal and GP still have not used up-to-date information and modern international treatment approach in the T2DM patient management.

Publications: There was no publish data for this report.