STUDY REPORT SYNOPSIS

REal World Assessment of Efficacy & Safety Parameters – Including Month of Ramadan - for Dapagliflozin in Management of Type II Diabetes Mellitus

Milestones:	12 months observational study with the administration of Dapagliflozin [sodium-glucose co-transporter-2 selective inhibitor] (Forxiga), 10 mg oral (without regards to meals) Once Daily (QD), morning or evening, taken ≥ four weeks and ≤ 24 weeks prior to the recruitment date.
Phase of development:	Phase (IV) 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.

Background/rationale:

Multi-center, post-authorization, prospective, open-label, non-interventional, real-life, observational, cohort study. The study was conducted at 11 sites in the UAE and Kuwait assessing the clinical outcome changes –including the month of Ramadan- for Dapagliflozin in Management of Type II Diabetes Mellitus.

Objectives:

1. Primary Objective: To describe the changes in HbA1c from baseline as a parameter for blood glucose control.

2. Secondary Objectives: To describe the changes from baseline in the following parameters:
- Total body weight.
- Total cholesterol, LDL-C, non-HDL-C and triglycerides
- Systolic and diastolic blood pressures

3. Other Objectives: To capture the frequency and incidence of the following reported adverse events:
- Hypoglycemic episodes.
- Volume Depletion,
- Genital infections.
- Urinary tract infections.

Study design:

Multi-center, post-authorization, prospective, open-label, non-interventional, real-life, observational, cohort study. The study was conducted at 11 sites in the UAE and Kuwait.

Anonymized data were collected on patient demographics, disease profile, concomitant medications, and outcomes. The demographic and disease information collected comprised patient age, gender, renal function, and baseline measurement of HbA1c, weight, BMI, and blood pressure.

Efficacy:

The mean change in HbA1c from mean baseline and at Month 12.
The mean changes from mean baselines and at Month12 in total body weight, total cholesterol, LDL-C, non-HDL-C, triglycerides, systolic and diastolic blood pressures.

Safety:

Adverse events reported by the patient/subject or noted by the Investigator. In addition, the frequency and incidence of hypoglycemic episodes, volume depletion, genital infections, and urinary tract infections as reported adverse events during the 12 months period of the study.

Study population:

A total of 511 Type 2 Diabetes Mellitus patients were initially enrolled in the study at baseline, from a total of 11 centers in UAE & Kuwait.

Inclusion criteria:

- Male and female participants, aged ≥18 years who were diagnosed with T2DM at presentation
- Patients treated with Dapagliflozin (as per routine care and in compliance with the locally approved prescribing information) for ≥four weeks and ≤24 weeks prior to the recruitment date
- Patients with CrCl > 60 ml/min or eGFR > 60 ml/min/1.73m2
- Patients provided written informed consent

Exclusion criteria:

- Patients with contraindications to Dapagliflozin, as per the locally approved prescribing information, will be excluded from the study.
- If participating in any clinical trial, the subject cannot take part in this study.
- Patients with clinically significant renal, hepatic, hematological, oncological, endocrine, psychiatric or rheumatic disease.
- Patients who have a disease with a life expectancy under one year.
- Patients with CrCI < 60 ml/min or eGFR < 60 ml/min/1.73 m2 should be excluded from the trial.
- No medical claims with a diagnosis (or procedure, where appropriate) indicative for pregnancy or childbirth in the baseline

Statistical methods:

This analysis is descriptive in nature, and no hypothesis was formulated or tested.
Efficacy endpoints including HbA1c, weight, BPs, and lipids were analyzed descriptively by time point. Change and percent change from baseline was reported. Descriptive statistics were used to represent demographics and baselines covariates across different patients recruited by each center.
Continuous variables were presented by mean and SD while the frequency was used for categorical data. The mean change from baseline and at Month 12 in primary and secondary continuous variables was studied using a paired t-test. Point estimates and 95% CI were calculated for the mean change from baseline.
A linear regression model was used to test for significant changes in the mean of primary and secondary variables at Month 12. Universal covariates, such as age and sex, clinically important covariates and significant covariates in the two by two linear regression were considered in the final model.

Results:

The primary efficacy evaluation was to describe the changes in HbA1c from baseline, as a parameter for blood glucose control. The study showed that HbA1c improved significantly

with a mean change of -0.88%. A total of 41.6% of patients reached an HbA1c level of less than 7. A total of 34.6% of patients with uncontrolled diabetes on enrolment (HbA1c levels above 7%) achieved glycemic control by the end of this study. Male patients showed better glycemic control than female patients by the end of the study. However, age and BMI showed no obvious effect on reaching glycemic control.

This study had various effects on the secondary outcomes observed in this study. Regarding blood pressure, there were an improvement in systolic pressures yet no change at all in diastolic, with a significant difference between young and old age groups. Patients' pulse rate also decreased significantly by time in all BMI groups, ages, and genders, by the end of this study.

Total body weight and BMI significantly decreased in this study. There was a significant change in both weight and BMI with time, in both genders and age groups.

Regarding renal functions, e-GFR in total was decreased by a 0.94% median change from baseline during the one-year duration of this study. Both age groups of patients, above and below 50 years of age, showed significant change with time in eGFR, the difference between groups, and interaction between groups and time.

There was a general improvement of the lipid profile of enrolled patients throughout the study except for triglycerides. Total cholesterol, HDL and LDL significantly improved with time in relation to gender, age, and BMI. As for the difference between the age, BMI and gender groups, only age showed a significant difference in all lipid parameters, while there was a significant difference between males and females in the HDL parameter as well.

One of the objectives of this study was to observe the frequency and incidence of hypoglycemic episodes, volume depletion, and genital infections. The most commonly reported adverse event was hypoglycemia, followed by urinary tract infection, where only one patient reported having volume depletion.

Around 83% of patients reported experiencing a mild adverse event, about 14% with a moderate adverse event. The most common adverse event in the study was hypoglycemia which occurred in about 68% of patients enrolled. A total of 81 of the hypoglycemic episodes were mild in nature, and only nine were moderate. Only four patients (2.8%) reported a serious event where only 2 of them required hospitalization. Almost 90% of the adverse events occurring in this study were recovered.