OBSERVATIONAL STUDY REPORT SYNOPSIS

Lead

Retrospective Study of Patients with Type 2 Diabetes Mellitus on Dapagliflozin Therapy in Taiwan

This was an observational, retrospective study to collect data from 18 medical centers. T2DM patients who were treated with dapagliflozin after dapagliflozin was reimbursed in Taiwan since May 1st 2016 with at least 6 months of follow-up in either monotherapy or combination with other antidiabetic therapy, were eligible to enter this study.

Milestones:	Not Applicable
Phase of development:	Not Applicable – Observational study
Sponsor:	AstraZeneca

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

Background/Rationale:

To investigate retrospectively the glycemic control profile of dapagliflozin (Forxiga®) in Taiwan in the real-world clinical practice

Objectives:

Primary objective:

•To assess the change from baseline (time to initiate dapagliflozin*) in HbA1c at 6 months

*: The baseline was defined as the time, within 3 months, prior to the subject receiving dapagliflozin.

Secondary objectives:

- To assess the reason of starting dapagliflozin as next-step therapy for T2DM subjects
- To assess the change from baseline in HbA1c at 3 months
- Percentage of subjects reaching HbA1c <7.0%, 7.0~8.0%, 8.0~9.0%, and >9.0% at 3 and 6 months
- To estimate the change in fasting plasma glucose (FPG) at 3 and 6 months
- To estimate the change in weight (in kilograms) at 3 and 6 months
- To estimate the change in blood pressure (systolic/diastolic, in mmHg) at 3 and 6 months
- To estimate the change in lipids at 3 and 6 months (total cholesterol, HDL, LDL and triglycerides, in mg/dL)

Study design:

This was a multicentre and retrospective observational study, enrolling patients exposed to dapagliflozin after dapagliflozin reimbursement in Taiwan since May 1st 2016, to evaluate real life clinical glycemic control profile of dapagliflozin in Taiwanese Type 2 diabetes mellitus patients treated on an outpatient basis in clinical practice setting.

Data source: This was an observational, retrospective study to collect data from 18 medical centers. These clinical sites were selected for sufficient T2DM patient pool to fulfill the recruitment timeline and with adequate resources.

Study population:

T2DM patients who were treated with dapagliflozin after dapagliflozin was reimbursed in Taiwan since May 1st 2016 with at least 6 months of follow-up in either monotherapy or combination with other anti-diabetic therapy, were eligible to enter this study.

Inclusion Criteria:

1. Age≥ 20 years old.

2. T2DM patient initiated dapagliflozin after May 1st 2016 as the second line or third line oral anti-diabetic therapy, either as add-on or switching from one to another. Or initiating dapagliflozin as adjunctive therapy for T2DM subjects treated with insulin.

3. Completed follow-up of at least 6 months regardless of continuation on dapagliflozin therapy.

4. Provide completed and signed written informed consents

Exclusion criteria:

1. Subjects with a history of SGLT2 inhibitor therapy other than dapagliflozin prior to Baseline.

2. Subjects with Type 1 diabetes.

3. Treatment with other investigational drugs concurrently during the retrospective data collection period.

Statistical methods:

Two sets of population were used for the statistical analyses in the present study, including the per-protocol set (PPS) and the full analysis set (FAS).

The per-protocol set included all recruited subjects who met all inclusion and exclusion criteria, received at least one dose of dapagliflozin, and had HbA1c data at baseline and Month 6. This was the primary analysis population for the following variables: HbA1c, FPG, lipid profiles, body weight, and blood pressure.

The full analysis set included all subjects who had received at least one dose of dapagliflozin with at least one post-baseline assessment. This population was used for sensitivity analysis of primary outcome variable, the mean change from baseline in HbA1c level.

Results:

Totally 1987 subjects were enrolled and 1735 subjects were included in the FAS population whereas 1351 subjects were included in the PPS population. Of 1735 subjects, 1722 subjects (99.25 %, 1722/1735) were enrolled without violating eligibility criteria and initiated dapagliflozin after 01-May-2016.

The primary objective was to determine the change from baseline of HbA1c at Month 6. Results in this study demonstrated that mean HbA1c levels were significantly reduced by 0.66± 1.233% from baseline in the PPS.

The secondary objectives were to determine the followings:

(1) To assess the reason of starting dapagliflozin as next-step therapy for T2DM subjects

Results in this study demonstrated that major reasons of starting dapagliflozin as the anti-diabetic therapy included for the HbA1c lowering efficacy (0.66% at Month 6), followed by for lower weight gain concern (body weight decrease by 1.45 kg at Month 6), and for hypoglycaemia risk concern.

(2) To assess the change from baseline in HbA1c at 3 months

Results in this study demonstrated that mean HbA1c levels were significantly reduced by 0.59±1.098% from baseline at Month 3 in the PPS.

(3) Percentage of subjects reaching HbA1c <7.0%, 7.0~8.0%, 8.0~9.0% and >9.0% at 3 and 6 months

More than 50% of subjects had baseline HbA1c levels >8%. However, after initiating dapagliflozin at Month 3, more than 50% of subjects had HbA1c levels <8%. Similar results were observed at Month 6 in the present study.

(4) To estimate the change in fasting plasma glucose (FPG) at 3 and 6 months

Results in this study demonstrated that initiating dapagliflozin treatment significantly reduced the mean FPG levels (by 24.7 and 26.4 mg/dL at Months 3 and 6, respectively), in the PPS.

(5) To estimate the change in weight (in kilograms) at 3 and 6 months

Results in this study demonstrated that dosing with dapagliflozin significantly reduced the body weight (by 1.16 and 1.45 kg at Months 3 and 6, respectively) in the PPS.

(6) To estimate the change in blood pressure (systolic/diastolic, in mmHg) at 3 and 6 months

Dosing with dapagliflozin significantly reduced the blood pressure (SBP: 3.5 and 3 mmHg and DBP: 1.4 and 1.3 mmHg, at Months 3 and 6, respectively), though subjects appeared to be pre-hypertensive as the mean baseline SBP was greater than 120 mmHg in the PPS.

(7) To estimate the change in lipids at 3 and 6 months (Total cholesterol, HDL, LDL and triglycerides, in mg/dL)

Results in this study demonstrated that dosing with dapagliflozin significantly increased the levels of total cholesterol (4.5 and 2.8 mg/dL at Months 3 and 6, respectively), HDL (1.18 and 2.38 mg/dL, at Months 3 and 6, respectively), and LDL (2.26 and 0.86 mg/dL at Months 3 and 6, respectively), but significantly decreased the levels of triglyceride (4.2 and 17.73 mg/dL at Months 3 and 6, respectively) in the PPS.

Conclusion:

Results showed that initiating dapagliflozin treatment at 5 or 10 mg per day for 6 months significantly reduced the HbA1c levels (0.66%) in T2DM patients in the observational study as in the real world clinical practice. Significant decreases in FPG levels were also observed with 6-month of dapagliflozin dosing in the present study. These results demonstrated the efficacy of dapagliflozin for lowering the HbA1c levels in Taiwan. The major reasons for local investigator to choose dapagliflozin included its HbA1c lowering efficacy, followed by for lower weight gain concern, and for hypoglycaemia risk concern.