# STUDY REPORT SYNOPSIS

# Usage of Dapagliflozin - a Sodium Glucose Co-transporter inhibitor, in the management of Type-2 Diabetes Mellitus: A real world evidence study in Egyptian patients

**Milestones:**

Date of the first patient in (FPI): 9 March 2019
Date of last patient in (LPI): 28 December 2019
Date of last patient last visit (LPLV): 28 March 2020
Date of database lock: 28 September 2020

**Phase of development:**

Observational

**Sponsor:**

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





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**Background/rationale:**

Approximately 54.8 million people adults aged 20-79 are living with diabetes in the MENA region in 2019; Egypt is number 9 in the top 10 countries in the number of adults with diabetes (8.9 million), where Egypt represents 16.2% of the Diabetics in the MENA region (1). If not properly controlled, diabetes and its complications can result in frequent hospital admissions and premature death. Therefore, many studies are conducted annually to evaluate new antidiabetic medications. Metformin is used as 1st line oral antidiabetic drug in most cases. Sulfonylureas (SU) are used as a frequent first add-on after the failure of metformin monotherapy. Sodium-Glucose Co-transporter 2 (SGLT2) inhibitors are a newer class of therapy that has a lower incidence of hypoglycemia and, in addition, helps in Weight and BP reduction. In Egypt, SGLT2 inhibitors were introduced in 2016. It is not yet widely used for various reasons, including lack of wide clinical experience in Egyptian patients and safety concerns particularly related to infections and some rare Diabetic Ketoacidosis (DKA). Also, usage of SGLT2 inhibitors is limited in the early stage of diabetes as they are usually preferred as 3rd or 4th add-on therapy.

The existing dapagliflozin phase-3 clinical trial program on SGLT2 inhibitors didn't include subjects from Egypt. There is no study available that evaluates the effect of dapagliflozin in the real world scenario in Egypt. Key opinion leaders in diabetes in Egypt have also identified the need for study on Egyptian subjects to observe the usage pattern and effect of dapagliflozin, an SGLT2 inhibitor, in this specific real-world setting. Therefore, there is a need for data on real-world settings across Egypt. With this aim in mind, the present study has been planned.

**Objectives:**

**Primary Objective**

1- To describe baseline characteristics of patients starting dapagliflozin together with other antidiabetic medications, alone or in combination. And to describe if dapagliflozin was given as 2nd line, 3rd line, or later in combination therapy.

**Secondary Objectives**

1- To record the mean change in HbA1C from baseline to months 3 and 6.

2- To record the HbA1c change (%) as per different baseline HbA1c levels (<8%, 8-10%, and >10%).



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3- To record the percentage of patients achieving the HbA1c target (less than or equal to 7 %)

4- To record the change in weight (kg) as per different baseline BMI (kg/m2) (<25, 25-30, >30).

5- To record the change in blood pressure (mmHg) from baseline.

**Study design:** This study was a non-interventional, multicenter, retrospective-prospective, observational study conducted at up to 50 sites in Egypt. The study targeted to enrol 200 patients. The study was initiated after obtaining written approval from the Independent Ethics Committee (IEC) /Institutional Review Board (IRB) and written informed consent of the patient.

**Data source:** For the recruitment process, each investigator prepared a list of patients who were initiated on dapagliflozin after three months (± 30 days) prior to study initiation and selecting the patients consecutively as per eligibility criteria to avoid any selection bias. After the patients were found to be eligible and provide the written informed consent, baseline (retrospective) data were collected from the past medical records (demographic information, weight, height, BP, duration of diabetes, heart rate, medical & surgical history with relevant lab reports, HBA1c data, dapagliflozin was given as 2nd line or 3rd line as a monotherapy or in combination, Ramadan fasting status, and concomitant medications). For Baseline prospective data, after three months (± 30 days), data were collected for weight, height, BP, heart rate, HBA1c, Dapagliflozin administration, concomitant medications, and any AEs.

**Study population:** In the present multicentre prospective study, 195 patients were screened and enrolled with inadequately controlled T2DM (HbA1c >7%) with existing antidiabetic medications and who have been prescribed Dapa at least three months prior to study initiation. All patients presented at visit 1 (3-month from the baseline). At the end of the sixth month of follow-up, the HbA1c values were missed for only one patient.

**Inclusion criteria:**

1- Male or female patients with 18 years and above.

2- Patients who provide written, informed consent.

3- Patients with previously diagnosed Type-2 diabetes mellitus.



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4- Patients with inadequately controlled diabetes (HbA1c>7%) with existing antidiabetic medications, prior to initiation of dapagliflozin treatment.

5- Patients who initiated Dapagliflozin at least three months prior to the date of the study start.

6- Patients who are having past medical records for demographic information, Weight, blood pressure, HbA1c value, and concomitant medications at the time of Dapagliflozin prescribed.

**Exclusion Criteria**

1- Patients with Type-1 diabetes mellitus.

2- Patients with any medical condition which in the opinion of the investigator would interfere with safe completion of the study

3- Pregnant or lactating women

4- Patients with other severe conditions/elements which require / may require hospitalization during the study participation period.

**Statistical methods:** Data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 23. The Kolmogorov-Smirnov test and Shapiro-Wilk test explored the assumption of normality of the continuous variables. Summary statistics consist of the number and percentage of responses in each category for discrete variables and the mean, median, standard deviation, minimum, maximum, and interquartile range for continuous variables. The change of HbA1c, Weight, height, BMI, SBP, DBP, and HR from baseline to the 3-month and 6-month follow-up visits was described by a continuous summary. The difference was tested using the Wilcoxon signed-rank test and the Friedman test. $Chi^2$ was performed to evaluate the difference between categorical variables. Data were presented with their 95% confidence interval for the estimate of the parameter, where applicable.

**Results:** A total of 195 patients were recruited to the study from 33 sites in Egypt. All patients are Egyptians (99.5%) expect one Syrian patient (0.5%). Overall, there were slightly more males (57.9%) as compared to females (42.1%), with a mean± SD age of 54.33± 8.22 years. The average patients' weight, height, and BMI were 95.10±12.77 Kg, 168.96±7.56 cm, and 33.40±4.75 $kg/m^2$, respectively. In terms of BMI classification, 3 (1.62%) patients were normally weighted, 41 (22.16%) were over-weighted, and 141 (76.21%) were obese. Regarding the clinical characteristics, the average of T2DM duration was 8.18±5.46 years. At

baseline, the average of patients' SBP, DBP, and HR was 132.0± 12.50 mmHg, 81.95±7.20 mmHg, and 79.47±7.65 beat/min, respectively. All of the included patients received dapagliflozin from baseline to visit 1, while at visit 2, one patient was recorded as a loss of follow-up, and one patient discontinued the medication due to uncontrolled diabetes. At the baseline, 175 (89.7%) patients received dapagliflozin in combination with other medication such as Incretin mimetics (3.08%), Thiazolidinediones (2.3%), Insulins (3.59%), Insulin (16.9%), Dipeptidyl peptidase-4 inhibitors (17.4%), Sulfonylureas (45.6%), and Biguanides (49.2%). In about 61.5% of the included patients, dapagliflozin was administrated as a third line, and in 38.5%, it was administrated as a second line of treatment. Almost the majority of patients (91.8%) were received dapagliflozin 10 mg, and only (8.2%) received dapagliflozin 5 mg. After three months from the baseline, the level of HbA1c was reduced in 181 patients with a mean difference of (MD= -1.28, 95% CI: -1.42, -1.14), resulting in achieving adequate control (<7%) of HbA1c in 28.20%, 95% CI (21.9%, 34.5%). At visit 2, the level of HbA1c was reduced in 189 patients with a mean difference of (MD= -1.77, 95% CI: -1.95, -1.60), resulting in achieving adequate control (<7%) of HbA1c in 50%, 95% CI (43.0%, 57.0%) of the patients, compared to baseline. Compared to visit 1, the level of HbA1c at visit 2 was decreased with a significant difference (MD= -0.50, 95% CI: -0.60, -0.40). Regarding the weight, 150 (76.92%) patients showed a significant reduction in their weight at visit 1 compared to the baseline (MD= -3.33, 95% CI: -3.94, -2.71). At the visit 2, about 173 (89.71%) patients showed a significant weight reduction compared to the baseline (MD= -5.46, 95% CI: -5.46, -6.39). Similarly, in comparison with visit 1, 129 (66.49%) patients at the visit 2 showed a significant weight reduction (MD= -2.16, 95% CI: -2.86, -1.44). 16 (8.2%) patients had experienced adverse events. Only one patient was recorded as a loss during the follow-up at visit 2, and one patient discontinued the medication due to uncontrolled diabetes. In terms of the severity of the reported adverse events, 8 (44.4%) were mild, and 10 (55.6%) were moderate. In terms of drug-related adverse events, 13 (72.2%) of the reported adverse events were related to the drug. The most common reported adverse event was urinary tract infection (3.58%), followed by headache (1.02%), toothache (1.02%), and gastritis (0.51%).

**Conclusion:** [redacted]



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**Publications:**


- *Gorgojo-Martínez JJ, Serrano-Moreno C, Sanz-Velasco A, Feo-Ortega G, Almodóvar-Ruiz F. Real-world effectiveness and safety of dapagliflozin therapy added to a GLP1 receptor agonist in patients with type 2 diabetes. Nutr Metab Cardiovasc Dis [Internet]. 2017 Feb;27 (2):129–37. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0939475316301995*
- *Bolinder J, Ljunggren Ö, Johansson L, Wilding J, Langkilde AM, Sjöström CD, et al. dapagliflozin maintains glycaemic control while reducing weight and body fat mass over 2 years in patients with type 2 diabetes mellitus inadequately controlled on metformin. Diabetes, Obes Metab [Internet]. 2014 Feb;16 (2):159–69. Available from: http://doi.wiley.com/10.1111/dom.12189*
- *Kostev K, Pscherer S, Rist R, Busch S, Scheerer MF. Changes in Glycemic Control and Body Weight After Initiation of Dapagliflozin or Basal Insulin Supported Oral Therapy in Type 2 Diabetes: A Primary Care Database Study. J Diabetes Sci Technol [Internet]. 2017 4 May;11(3):590–6. Available from: http://journals.sagepub.com/doi/10.1177/193229681668*
- *Wilding J, Bailey C, Rigney U, Blak B, Beekman W, Emmas C. Glycated Hemoglobin, Body Weight and Blood Pressure in Type 2 Diabetes Patients Initiating Dapagliflozin Treatment in Primary Care: A Retrospective Study. Diabetes Ther [Internet]. 2016 Dec 1;7(4):695–711. Available from: http://link.springer.com/10.1007/s13300-016-0193-8*
- *Bailey CJ, Gross JL, Pieters A, Bastien A, List JF. Effect of dapagliflozin in patients with type 2 diabetes who have inadequate glycaemic control with metformin: a randomised, double-blind, placebo-controlled trial. Lancet [Internet]. 2010 Jun;375(9733):2223–33. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673610604072*
- *Del Prato S, Nauck M, Durán-Garcia S, Maffei L, Rohwedder K, Theuerkauf A, et al. Long-term glycaemic response and tolerability of dapagliflozin versus a sulphonylurea as add-on therapy to metformin in patients with type 2 diabetes: 4-year data. Diabetes, Obes Metab [Internet]. 2015 Jun 6;17(6):581–90. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/dom.12459*
- *Sun YN, Zhou Y, Chen X, Che WS, Leung SW. The efficacy of dapagliflozin combined with hypoglycaemic drugs in treating type 2 diabetes mellitus: Meta-analysis of randomised controlled trials. BMJ Open. 2014*




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