DEPICT-1 Study

Internal Use Only

farxiga® (dapagliflozin) 5mg tablets

Study **Objective**

SGLT2 inhibitors are widely used in T2D. Prior studies had suggested potential benefits of SGLT2 inhibitors in T1D, but also raised safety concerns, particularly around DKA. DEPICT-1 was designed to assess whether the addition of the SGLT2 inhibitor dapagliflozin (5 mg or 10 mg once daily) to adjustable insulin can safely improve glycemic control in adults with inadequately controlled T1D.

Study **Design** 24-week duration

Multicenter, double-blind, randomized, parallel-controlled, 3-arm, phase 3 study

1:1:1 randomization:
DAPA (5 mg) + insulin (n = 277)
DAPA (10 mg) + insulin (n = 296)
Matched placebo + insulin (n = 260)

8-week lead-in period to optimize diabetes management

24-week active treatment phase*

28-week extension phase to assess longer-term safety (not reported here)

*After the first dose of the study drug, the total insulin dose was recommended to be reduced symmetrically in basal and bolus insulin by up to 20% to minimize the risk of hypoglycemia before subsequently titrating back to as close to baseline level as possible.

Conducted at **143 sites** in **17 countries**
(Australia, Austria, Belgium, Canada, Germany, Denmark, Finland, France, Hungary, Israel, Italy, Mexico, Romania, Spain, Sweden, the UK, and the USA)

Baseline A1C = **7.5%–10.5%**
(58.5–91.3 mmol/mol)
Patients were 18–75 years of age with inadequately controlled T1D after being on insulin therapy for ≥ 12 months.

Primary **efficacy endpoint:**

Change from baseline in A1C after 24 weeks in the full analysis set†

† Full analysis set comprised of all randomly assigned individuals who received one dose of the study drug.

Secondary **efficacy endpoints**‡**:**

- % change in total daily insulin
- % change in body weight
- Proportion of patients achieving 0.5% A1C reduction without severe hypoglycemic events

‡ See published study for full list of secondary efficacy endpoints

Abbreviations: A1C, glycated hemoglobin A1c; DAPA, dapagliflozin; DKA, diabetic ketoacidosis; SGLT2, sodium glucose cotransporter-2; T1D, type 1 diabetes; T2D, type 2 diabetes.

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Safety Assessment

Safety and tolerability were assessed in the safety analysis set*

*Safety analysis set consisted of all patients who took at least one dose of study medication, including 55 incorrectly randomized patients who were not included in the full analysis set.

In addition to hypoglycemia and DKA, AEs of special interest included: liver dysfunction, kidney dysfunction, UTI, genital infections, fractures, volume depletion, hypersensitivity reactions, and CV-related AEs

Key Inclusion Criteria

- Patients 18–75 years of age who had:
  - Inadequately controlled T1D (7.7%–11.0% at screening; 7.5%–10.5% at randomization)
  - Taking insulin >12 months

Baseline Parameters Required for Inclusion	
C-peptide (ng/mL)	<0.7
BMI (kg/m^2)	≥18.5

Key Exclusion Criteria

History of diabetes types other than T1D, chronic pancreatitis or other pancreatic disorders resulting in decreased beta-cell capacity

Frequent episodes of severe hypoglycemia or hospitalized for hyperglycemia or hypoglycemia within 1 month prior to screening; signs/symptoms of poor glycemic control; prior use of an SGLT2 inhibitor

Baseline Patient Characteristics

	DAPA (5 mg) + insulin	DAPA (10 mg) + insulin	Placebo + insulin
Male (%)	43	50	51
Mean age (years)	41.9	42.7	42.7
Bodyweight (kg)	80.8	82.0	84.3
Duration of T1D (years)	19.7	19.9	21.2
A1C (%)	8.53	8.52	8.53

Mean BMI: **28.3 kg/m^2**
Mean insulin dose: **61.6 IU**

Method of insulin administration:
63% MDI / 37% CSII / 33% CGM

A1C at randomization:
~75% **≥7.5% to <9.0%**
~25% **≥9.0% to <10.5%**

Abbreviations: A1C, glycated hemoglobin A1c; AE, adverse event; BMI, body mass index;; CGM, continuous glucose monitoring; CSII, continuous subcutaneous insulin infusion; CV, cardiovascular; DAPA, dapagliflozin; DKA, diabetic ketoacidosis; IU, insulin units; MDI, multiple daily injections; SGLT2, sodium glucose cotransporter-2 ; T1D, type 1 diabetes; UTI, urinary tract infection.

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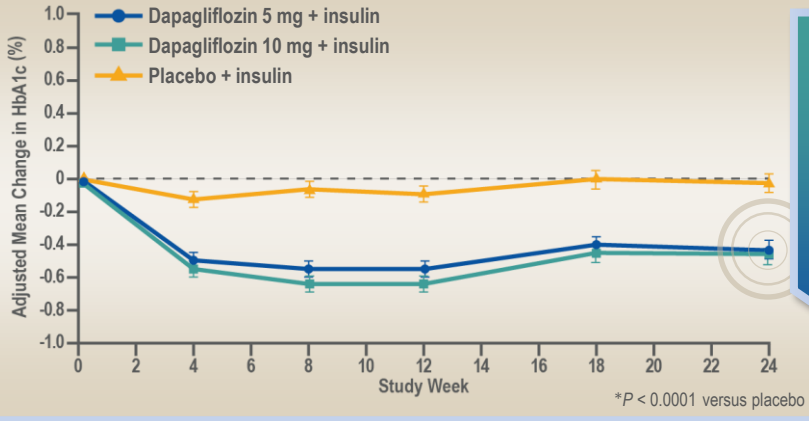
Study Results

Primary Endpoint

Change in A1C Over 24 Weeks



-0.42% DAPA (5 mg)*

-0.45% DAPA (10 mg)*

Secondary Endpoints

†*P* < 0.0001 versus placebo

Mean Change in Total Daily Dose of Insulin vs Placebo

DAPA (5 mg) **-8.8%**†

DAPA (10 mg) **-13.2%**†

Mean Change in Bodyweight vs Placebo

-2.96% DAPA (5 mg)†

-3.72% DAPA (10 mg)†

Proportion With ≥0.5% A1C Reduction and No Severe Hypoglycemic Episodes

50% DAPA (5 mg)†

51% DAPA (10 mg)†

25% placebo

Incidence of Treatment-related Adverse Events (AEs)

29% of patients DAPA (5 mg) + insulin

28% of patients DAPA (10 mg) + insulin

12% of patients placebo + insulin

Most Commonly Reported AEs

- Nasopharyngitis, UTI, upper respiratory tract infection, and headache

Discontinuations Due to AEs

- Hypoglycemia and severe hypoglycemia was not increased in the treatment groups
- **Similar numbers of patients had definite DKA events** (rates of possible or unlikely DKA were increased with DAPA)‡

‡Missed insulin dose and insulin pump failure were the most common causes of DKA.

Study Summary

- Improved glycemic control
- Sustained weight loss
- Insulin dose reduction
- No new safety signals (including incidence of DKA)

Abbreviations: A1C, glycated hemoglobin A1c; AE, adverse event; DAPA, dapagliflozin; DKA, diabetic ketoacidosis; T1D, type 1 diabetes; UTI, urinary tract infection.