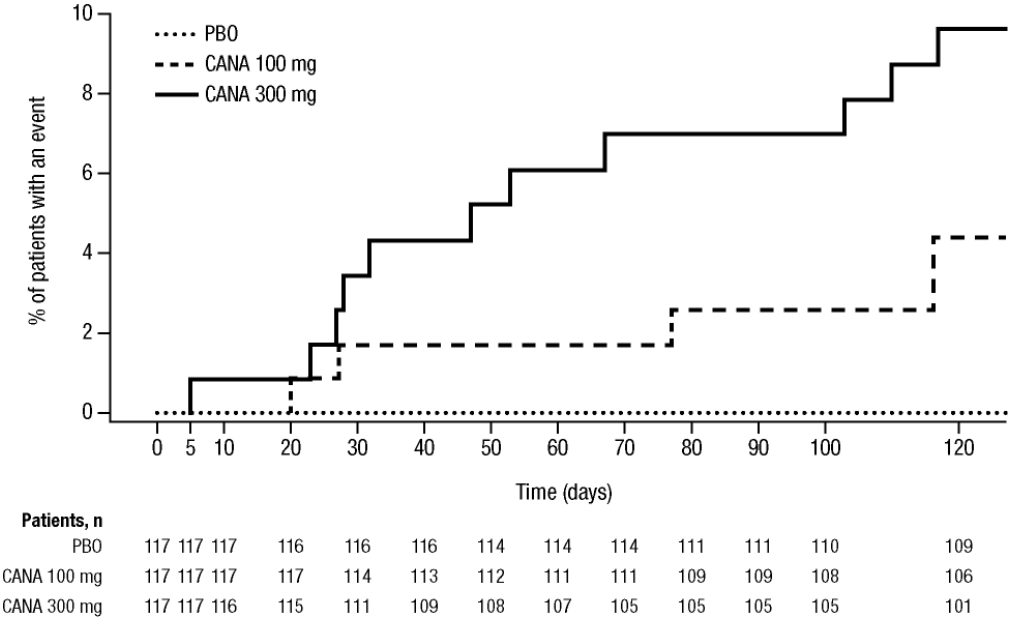
SUPPLEMENTARY DATA

Supplementary Figure 1. Kaplan-Meier plot of time to first ketone-related AE.



Patients, n													
PBO	117	117	117	116	116	116	114	114	114	111	111	110	109
CANA 100 mg	117	117	117	117	114	113	112	111	111	109	109	108	106
CANA 300 mg	117	117	116	115	111	109	108	107	105	105	105	105	101

AE, adverse event; PBO, placebo; CANA, canagliflozin.

SUPPLEMENTARY DATA

Supplementary Information. Guidelines for the Diagnosis, Treatment, and Prevention of DKA Provided in the Study Protocol

Guidelines for Diagnosis, Treatment and Prevention of DKA

The guidelines for diagnosis, treatment and prevention of DKA presented below are based on the American Diabetes Association (ADA) recommendations. They are provided here as suggested guidelines, but investigators should use their clinical judgment in monitoring patients for and treating DKA.

Recognition of DKA

Early Symptoms

- Thirst or a very dry mouth
- Frequent urination
- High blood glucose (blood sugar) levels
- High levels of ketones in the urine

Later Symptoms

- Constantly feeling tired
- Dry or flushed skin
- Nausea, vomiting, or abdominal pain (vomiting can be caused by many illnesses, not just ketoacidosis. If vomiting continues for more than 2 hours, contact your health care provider)
- Difficulty breathing
- Fruity odor on breath
- A hard time paying attention, or confusion

Monitoring for Ketones

Patients should be instructed to monitor their urine for ketones every 4 to 6 hours when:

- Blood glucose ≥240 mg/dL (≥13.3 mmol/L)
- During illness
- In the presence of symptoms of DKA

Suggested Guidelines for Subject Sick Day Management

The guidelines for sick day management presented below are based on the established ADA recommendations for the sick day management of patients with T1DM. They are provided here as suggested guidelines to be used by investigators when counseling subjects. Investigators are expected to manage their subjects based on their clinical judgment, knowledge of the subject's medical history, and their established paradigms within their clinical practice for the management of ill T1DM patients.

Monitoring

- Blood glucose and urine (or blood) ketones need to be tested frequently during illness, often every 2 to 4 hours
- Patients should test their urine for ketones if:
    - They have a blood glucose value >250 mg/dL (>13.9 mmol/L) that cannot otherwise be explained
    - They feel ill, even if their blood glucose values are normal

- Patients should call the study site if their pre-prandial blood glucose values remain >250 mg/dL (>13.9 mmol/L) or they measure moderate to high ketone values

Insulin

- Patients should be instructed to continue their insulin dosage even if they are vomiting and unable to eat. Supplemental insulin (ie, correction bolus) may be required depending on the patient's blood glucose measurements

Food and fluid intake

- Patients should be instructed to eat small meals and to eat more frequently when they are ill. Soft foods or liquids are often tolerated best. Eating about 10 to 15 grams of carbohydrate every 1 to 2 hours is usually sufficient. Foods and beverages containing about 15 grams of carbohydrate that can be recommended to patients include:
  - ½ cup (~ 125 ml) regular gelatin
  - ½ cup (~ 125 ml) ice cream
  - ½ cup (~ 125 ml) custard
  - 1 regular double popsicle
  - ¾ cup (~ 200 ml) regular ginger ale
  - ½ cup (~ 125 ml) regular soft drink
  - ½ cup (~ 125 ml) orange or apple juice
  - 1 cup (~ 250 ml) Gatorade
  - 1 cup (~ 250 ml) creamed soup

Fluid intake is essential during illness. If vomiting, diarrhea, or fever is present, the patient should be instructed to take small quantities of liquids every 15 to 30 minutes. Clear broth, tea, or other fluids can supplement liquids containing carbohydrate.

Patients should seek medical attention when they have:

- Fever >100^{o} F (37.8° C)
- Persistent diarrhea
- Vomiting and unable to take fluids for >4 hours
- Blood glucose levels that are difficult to control with or without ketones (see information on monitoring)
- Severe abdominal pain
- Other unexplained symptoms
- Illness that persists over 24 hours