**Transcript Details**
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Renal and Cardiovascular Outcomes in Adults With Diabetic Nephropathy (ie, DKD) and Type 2 Diabetes

**Dr Caudle:**
I'm your host, Dr Jennifer Caudle, and joining me today is Dr Gates Colbert, a nephrologist from Baylor Medical Center in Dallas, Texas.

Today, we will be discussing INVOKANA®, or canagliflozin, the first therapy in approximately 20 years approved to treat diabetic nephropathy, or diabetic kidney disease, in adults with type 2 diabetes and albuminuria greater than 300 mg per day. [1-5,7] INVOKANA® carries three indications. It was initially approved in 2013 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. In 2018, INVOKANA® received an indication to reduce the risk of major adverse cardiovascular events, or MACE, which include cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke in adults with type 2 diabetes mellitus and established cardiovascular disease[7]. In 2019, INVOKANA® received its latest indication to reduce the risk of end-stage kidney disease or ESKD, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day.

INVOKANA® is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients. INVOKANA® is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 $m^2$. INVOKANA® is likely to be ineffective in this setting based upon its mechanism of action.[7]

INVOKANA® is contraindicated in patients with serious hypersensitivity reaction to INVOKANA®, such as anaphylaxis or angioedema, and in patients on dialysis.

Please read and listen to the Important Safety Information presented in this video. Additionally, please read the full Prescribing Information and Medication Guide available at www.Invokana.com/PI.

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Dr Colbert, thank you so much for joining us.

**Dr Colbert:**
Yes, thank you Dr. Caudle!

**Dr Caudle:**
Can you tell us about the CREDENCE trial, which is the first completed, dedicated SGLT2-inhibitor trial studying renal outcomes as the primary endpoint exclusively in patients with DKD and type 2 diabetes?[5,8,9]

**Dr Colbert:**
Sure, absolutely. The CREDENCE trial was one of the most important trials that came out in the nephrology community in 2019. This trial was notable data for us to help our patients with type 2 diabetes and diabetic kidney disease, also known as DKD.

CREDENCE, or Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation, was a randomized, placebo-controlled, double-blind, parallel group, multicenter, event-driven clinical trial comparing the effects of INVOKANA® 100 mg versus placebo in 4401 men and women with type 2 diabetes and chronic kidney disease.[5] For this trial, patients who had an eGFR of

30 to less than 90 mL/min/1.73 $m^2$, or eGFR units, and albuminuria of greater than 300 to 5000 mg/g and were already taking a stable, maximum-tolerated or labeled dose for 4 or more weeks prior to randomization of an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker were recruited.[5] The mean eGFR of patients was 56.2 eGFR units, and the median urinary albumin-to-creatinine ratio was 927 mg/g.[5]

The primary efficacy outcome was the composite of end-stage kidney disease, defined as dialysis, transplant, or sustained eGFR of less than 15 eGFR units, doubling of serum creatinine, or renal death or cardiovascular death.

The results of the primary composite outcome showed a 30 percent relative risk reduction with INVOKANA® 100 mg compared to placebo[5] *(Placebo (Event rate: 6.1 [per 100 patient-years]) INVOKANA® 100 mg (Event rate: 4.3 [per 100 patient-years])).*

Prespecified secondary outcomes included a composite of cardiovascular death or hospitalization for heart failure, which showed a 31 percent relative risk reduction versus placebo *(Placebo (Event rate: 4.5 [per 100 patient-years]) INVOKANA® 100 mg (Event rate: 3.2 [per 100 patient-years]))*; a composite of heart attack, stroke, or cardiovascular death, which showed a 20 percent relative risk reduction versus placebo *(Placebo (Event rate: 4.9 [per 100 patient-years]) INVOKANA® 100 mg (Event rate: 3.9 [per 100 patient-years]))*; hospitalization for heart failure, which showed a 39 percent relative risk reduction versus placebo *(Placebo (Event rate: 2.5 [per 100 patient-years]) INVOKANA® 100 mg (Event rate: 1.6 [per 100 patient-years]))*; and a composite of end-stage kidney disease, doubling of the serum creatinine, or renal death, which showed a 34 percent relative risk reduction versus placebo *(Placebo (Event rate: 4.0 [per 100 patient-years]) INVOKANA® 100 mg (Event rate: 2.7 [per 100 patient-years]))*. The difference in the decline in chronic eGFR slope was 2.74 eGFR units per year with a 95 percent confidence interval of 2.3 to 3.11 over 3.5 years for INVOKANA® versus placebo. This was an exploratory outcome.[5]

Turning to the safety data, similar overall AEs with INVOKANA® versus placebo (35.1 versus 37.9 per 100 patient-years) were observed. Male GMI incidence was 0.84 versus 0.09 per 100 patient-years, respectively. DKA was 0.22 versus 0.02 per 100 patient-years, respectively. No imbalance in fracture or amputation was found. Hypotension incidence was 2.8 percent versus 1.5 percent, respectively. Hypoglycemia was 4.43 versus 4.89 per 100 patient-years, respectively.[5] There were similar rates of serious adverse events with INVOKANA® and placebo, that is, 14.5 versus 16.4 per 100 patient-years, respectively.[5] Additional reported adverse events of interest where there was no imbalance were urinary tract infections, hyperkalemia, volume depletion-related adverse events, acute kidney injury, breast cancer, bladder cancer, acute pancreatitis, and renal cell carcinoma.[5] There was no imbalance in amputation or fractures observed with INVOKANA® versus the placebo cohort in this trial.[5]

The CREDENCE trial ended early after the overall risks and benefits were assessed and clear evidence of efficacy and safety was shown.

Note that the early termination of the trial may limit the power of some secondary outcomes and increase the risk of overestimating effect sizes. Patients with eGFR less than 30 eGFR units with normoalbuminuria or microalbuminuria, as well as kidney diseases other than those related to diabetic kidney disease, were excluded from the study.[5]

CREDENCE is the first dedicated SGLT2 inhibitor trial to study renal outcomes as the primary endpoint exclusively in patients with diabetic kidney disease and type 2 diabetes.[5,8,9] Overall, it was a landmark trial looking at patients that we, as treating clinicians, are going to see every day in our clinics.

**Dr Caudle:**
Now, what specific clinical parameters do you look for when a patient with type 2 diabetes and diabetic kidney disease is referred to you?

**Dr Colbert:**
I always want to look at the creatinine and eGFR of patients with type 2 diabetes and diabetic kidney disease to determine where they are on their renal function staging. Even if the eGFR is acceptable, it doesn't mean that the patient isn't at risk for developing progressive diabetic kidney disease. I look at the urine albumin-creatinine ratio regularly to help me guide therapy.[21] And I always want to look at other comorbidities and their past medical history including any history of cardiovascular disease.[22]

I would also look at their lipid profile, obesity, and any history of smoking, and would want to make sure that the patient is on goal-directed therapy for diabetes, hypertension, and diabetic kidney disease.[22] So, that's going to include renin-angiotensin-aldosterone system inhibitors (RAAS) inhibitors, good glycemic and blood pressure control, and addressing any other comorbidities that may increase risks for a patient with type 2 diabetes and diabetic kidney disease.[2-4,21]

**Dr Caudle:**
Based on data from the landmark CREDENCE trial, INVOKANA® received an indication to reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy and albuminuria greater than 300 mg/day.[5,7] What is the significance of this indication to you and what do you think it can mean to your patients?

**Dr Colbert:**
I think that this is a noteworthy indication for INVOKANA® because it's addressing exactly what we're trying to do to help our patients. The patients in the CREDENCE trial were all on maximum-tolerated doses of RAAS inhibitors,[5] which is what we're supposed to be doing for goal-directed therapy. We would need not only to get prescribers to understand the benefits and risks, but also our patients as well. We know that this indication for INVOKANA® shows our patients that there is the potential to slow the progression to dialysis or, possibly, a kidney transplant.[7]

The CREDENCE trial outcomes were relevant to our practice because we want to slow the progression of patients to end-stage kidney disease. Treating patients with INVOKANA® can help achieve this outcome.[5] After the initial decline, the decline in chronic eGFR slope was less by 2.74 eGFR units per year (95 percent confidence interval of 2.3 to 3.11) over 3.5 years for INVOKANA® versus placebo. This was an exploratory endpoint.[5]

Once you start them on INVOKANA® 100 mg, the patient can stay on the same stable dose even if eGFR declines to 30 eGFR units and below 30 eGFR unitsif albuminuriais greater than 300 mg/day, to reduce the risk of end-stage kidney disease, doubling of serum creatinine, cardiovascular death, and hospitalization for heart failure, unless dialysis is initiated. INVOKANA® is contraindicated in patients on dialysis.[7] Later on I will provide background on the updated dosage recommendations for MACE in established cardiovascular disease and A1C indications.

As we know, patients with type 2 diabetes and diabetic kidney disease are at high risk of having a cardiovascular event.[14,23] INVOKANA® directly lowers the risk of a major adverse cardiovascular events and hospitalization for heart failure.[5] With INVOKANA®, we're directly addressing type 2 diabetes and diabetic kidney disease. And all of these benefits, including reduction in risk of major cardiovascular events or MACE, may help our patients achieve the clinical outcomes that we're trying to get.

As I mentioned previously, similar overall adverse events with INVOKANA® versus placebo (35.1 versus 37.9 per 100 patient-years) were observed. Male GMI incidence was 0.84 versus 0.09 per 100 patient-years, respectively. DKA was 0.22 versus 0.02 per 100 patient-years, respectively. No imbalance in fracture or amputation was found. Hypotension incidence was 2.8 percent versus 1.5 percent, respectively. Hypoglycemia was 4.43 versus 4.89 per 100 patient-years, respectively.[5,7] There were similar rates of serious adverse events with INVOKANA® and placebo (14.5 versus 16.4 per 100 patient-years, respectively).[5]

So, overall, it appears that this medication has a well-delineated safety profile for our patients.

**Dr Caudle:**
Ok. Now looking at the CREDENCE data, how does the study population[5] compare with the patients you see in your office?

**Dr Colbert:**
When we look at the study population compared to what I see in my clinic, I think it's very similar to what I'm seeing every day and to what I think most nephrologists encounter. Approximately 40 percent of end-stage kidney disease is caused by diabetes.[22] So, we're going to see a large number of patients in our clinics with type 2 diabetes and diabetic kidney disease.

**Dr Caudle:**
Ok. So, what are the typical characteristics of a patient for whom you might prescribe INVOKANA®? And when treating a patient with type 2 diabetes and diabetic kidney disease, when might you start INVOKANA®?

**Dr Colbert:**
If the patient has type 2 diabetes and DKD with albuminuria greater than 300 mg/day and an eGFR greater than or equal to 30 eGFR units, INVOKANA® can be initiated to reduce the risk of ESKD, cardiovascular death, and hospitalization for heart failure assuming it has not already been initiated for glycemic control or reducing risk of MACE in established cardiovascular disease. I would start INVOKANA® as soon as I recognize these variables in my patient. According to the label, you don't need to wait for the eGFR to decline to a certain level, below 60 or below 45, to prescribe INVOKANA® for a patient with type 2 diabetes and albuminuria greater than 300

mg/day, as long as the eGFR is at least 30 eGFR units.[5,7] INVOKANA® is contraindicated in patients on dialysis.[7] As a nephrologist, I am focused on treating the diabetic kidney disease in a patient with type 2 diabetes, and not on treating the glycemia, per se.

**Dr Caudle:**
And what might you tell another physician who treats patients with type 2 diabetes about INVOKANA® if he or she didn't know much about it? And how would you present the safety and efficacy profile from the CREDENCE trial?

**Dr Colbert:**
Physicians and providers have been trying to maximize RAAS inhibitors, and control the glucose levels and weight in patients with type 2 diabetes and diabetic kidney disease. And we have seen through these years that many patients' DKD continues to progress, even when treated with an ACE inhibitor or ARB. With INVOKANA®, we have an SGLT2 inhibitor that has data to prove there is a reduction in the risk of end-stage kidney disease and major adverse cardiovascular events and hospitalization for heart failure in patients already taking a maximum-tolerated dose of an ACE inhibitor or ARB. [5] The CREDENCE data showed a 30 percent relative risk reduction in the primary composite outcome of end-stage kidney disease, doubling of serum creatinine, and renal and cardiovascular death.[5] *(Placebo (Event rate: 6.1 [per 100 patient-years])[5] INVOKANA® 100 mg (Event rate: 4.3 [per 100 patient-years]))[5]* There was a 20 percent relative risk reduction in major cardiovascular events criteria, *(Placebo (Event rate: 4.9 [per 100 patient-years])[6] INVOKANA® 100 mg (Event rate: 3.9 [per 100 patient-years]))[6]* as well as a 39 percent relative risk reduction in hospitalization from heart failure as secondary outcomes.[7] *(Placebo (Event rate: 2.5 [per 100 patient-years])[6] INVOKANA® 100 mg (Event rate: 1.6 [per 100 patient-years]))[6]* The decline in eGFR slope was less by 2.74 eGFR units per year with a 95 percent confidence interval of 2.3 to 3.11 over 3.5 years for INVOKANA® versus placebo. This was an exploratory outcome.[5] There are also potential benefits of weight loss and improvements in blood pressure control as well, although INVOKANA® is not indicated for either of these—weight loss or blood pressure control.[5]

So, I would tell other physicians that similar overall adverse events with INVOKANA® versus placebo (35.1 versus 37.9 per 100 patient-years) were observed. Male GMI incidence was 0.84 versus 0.09 per 100 patient-years, respectively. DKA was 0.22 versus 0.02 per 100 patient-years, respectively. No imbalance in fracture or amputation was found. Hypotension incidence was 2.8 percent versus 1.5 percent, respectively. Hypoglycemia was 4.43 versus 4.89 per 100 patient-years, respectively. There were similar rates of serious adverse events with INVOKANA® and placebo (14.5 versus 16.4 per 100 patient-years, respectively).[5]

As I mentioned, there was no imbalance in amputation, fractures, or hypoglycemia observed with INVOKANA® versus the placebo in the CREDENCE trial.[5]

It's really nice to have an effective medication with good trial results showing we can initiate this medication as long as the eGFR is at least 30 eGFR units and the urine albumin to creatinine ratio is greater than 300 mg/day, where previously we may not have been able to do much if the eGFR was this low.

I would also like to note that INVOKANA® can be initiated down to 30 eGFR units for established cardiovascular disease as well as A1C regardless of albuminuria. Once initiated, 100-mg dosing can be continued as eGFR declines below 30 eGFR units in patients with albuminuria greater than 300 mg/day to reduce the risk of ESKD, doubling of serum creatinine, CV death, and hospitalization for heart failure, unless the patient has started on dialysis.[7] This medication provides notable benefits to many of our patients with type 2 diabetes and diabetic kidney disease.

**Dr Caudle:**
Thank you for summarizing the safety and efficacy data from the CREDENCE trial. Now let's review the full Important Safety Information.

**Announcer:**
**INDICATIONS**

INVOKANA® (canagliflozin) is indicated:

- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- to reduce the risk of major adverse cardiovascular events (cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke) in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD)

- to reduce the risk of end-stage kidney disease (ESKD), doubling of serum creatinine, cardiovascular (CV) death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria greater than 300 mg/day

Limitations of Use

INVOKANA® is not recommended in patients with type 1 diabetes mellitus. It may increase the risk of diabetic ketoacidosis in these patients.

INVOKANA® is not recommended for use to improve glycemic control in adults with type 2 diabetes mellitus with an eGFR less than 30 mL/min/1.73 $m^2$. INVOKANA® is likely to be ineffective in this setting based upon its mechanism of action.

**IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS**

- Serious hypersensitivity reaction to INVOKANA®, such as anaphylaxis or angioedema
- Patients on dialysis

**WARNINGS AND PRECAUTIONS**

- **Lower-Limb Amputation:** An increased risk of lower-limb amputations associated with INVOKANA® use versus placebo was observed in CANVAS (5.9 vs 2.8 events per 1000 patient-years) and CANVAS-R (7.5 vs 4.2 events per 1000 patient-years), two randomized, placebo-controlled trials evaluating patients with type 2 diabetes who had either established cardiovascular disease or were at risk for cardiovascular disease. The risk of lower-limb amputations was observed at both the 100-mg and 300-mg once-daily dosage regimens.

  Amputations of the toe and midfoot (99 out of 140 patients with amputations receiving INVOKANA® in the two trials) were the most frequent; however, amputations involving the leg, below and above the knee, were also observed (41 out of 140 patients with amputations receiving INVOKANA® in the two trials). Some patients had multiple amputations, some involving both lower limbs.

  Lower-limb infections, gangrene, and diabetic foot ulcers were the most common precipitating medical events leading to the need for an amputation. The risk of amputation was highest in patients with a baseline history of prior amputation, peripheral vascular disease, and neuropathy.

  Before initiating INVOKANA®, consider factors in the patient history that may predispose to the need for amputations, such as a history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers. Counsel patients about the importance of routine preventative foot care. Monitor patients for signs and symptoms of infection (including osteomyelitis), new pain or tenderness, sores, or ulcers involving the lower limbs, and discontinue if these complications occur.

- **Volume Depletion:** INVOKANA® can cause intravascular volume contraction, which may sometimes manifest as symptomatic hypotension or acute transient changes in creatinine. There have been postmarketing reports of acute kidney injury which are likely related to volume depletion, some requiring hospitalizations and dialysis, in patients with type 2 diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA®. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 $m^2$), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating INVOKANA® in patients with one or more of these characteristics, assess and correct volume status. Monitor for signs and symptoms of volume depletion after initiating therapy.

- **Ketoacidosis:** Ketoacidosis, a serious life-threatening condition requiring urgent hospitalization, has been identified in patients with type 1 and 2 diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA®. In placebo-controlled trials of patients with type 1 diabetes, the risk of ketoacidosis was increased in patients who received SGLT2 inhibitors compared to patients who received placebo. The risk of ketoacidosis may be greater with higher doses. Fatal cases of ketoacidosis have been reported in patients taking INVOKANA®. Before initiating INVOKANA®, consider factors in patient history that may predispose to ketoacidosis. For patients who undergo scheduled surgery, consider temporarily discontinuing INVOKANA® for at least 3 days prior to surgery. Monitor for ketoacidosis and temporarily discontinue in other clinical situations known to predispose to ketoacidosis. Ensure risk

factors for ketoacidosis are resolved prior to restarting therapy. Educate patients on the signs and symptoms of ketoacidosis and instruct patients to discontinue INVOKANA® and seek medical attention immediately if signs and symptoms occur.

- **Urosepsis and Pyelonephritis:** Serious urinary tract infections, including urosepsis and pyelonephritis, requiring hospitalization have been reported in patients receiving SGLT2 inhibitors, including INVOKANA®. Treatment with SGLT2 inhibitors increases this risk. Evaluate for signs and symptoms and treat promptly.

- **Hypoglycemia With Concomitant Use With Insulin and Insulin Secretagogues:** Insulin and insulin secretagogues are known to cause hypoglycemia. INVOKANA® may increase the risk of hypoglycemia when combined with insulin or an insulin secretagogue. Therefore, a lower dose of insulin or insulin secretagogue may be required to minimize the risk of hypoglycemia when used in combination with INVOKANA®.

- **Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Necrotizing fasciitis of the perineum, a rare but serious and life-threatening necrotizing infection requiring urgent surgical intervention, has been identified in postmarketing surveillance in female and male patients with diabetes mellitus receiving SGLT2 inhibitors, including INVOKANA®. Serious outcomes have included hospitalization, multiple surgeries, and death. If suspected, start treatment immediately with broad-spectrum antibiotics and, if necessary, surgical debridement. Discontinue INVOKANA®.

- **Genital Mycotic Infections:** INVOKANA® increases risk of genital mycotic infections, especially in uncircumcised males or patients with prior infections. Monitor and treat appropriately.

- **Hypersensitivity Reactions:** Hypersensitivity reactions, including angioedema and anaphylaxis, were reported with INVOKANA®; these reactions generally occurred within hours to days after initiation. If reactions occur, discontinue INVOKANA®, treat, and monitor until signs and symptoms resolve.

- **Bone Fracture:** Increased risk of bone fracture, occurring as early as 12 weeks after treatment initiation, was observed in patients using INVOKANA®. Prior to initiation, consider factors that contribute to fracture risk.

DRUG INTERACTIONS

- **UGT Enzyme Inducers:** Co-administration with rifampin lowered INVOKANA® exposure, which may reduce the efficacy of INVOKANA®. For patients with eGFR ≥60 mL/min/1.73 $m^2$, if an inducer of UGTs (eg, rifampin, phenytoin, phenobarbital, ritonavir) is co-administered with INVOKANA®, increase the dose to 200 mg (taken as two 100 mg tablets) once daily in patients currently tolerating INVOKANA® 100 mg. The dose may be increased to 300 mg once daily in patients currently tolerating INVOKANA® 200 mg and who require additional glycemic control.

  For patients with eGFR <60 mL/min/1.73 $m^2$, if an inducer of UGTs is co-administered with INVOKANA®, increase the dose to 200 mg (taken as two 100 mg tablets) once daily in patients currently tolerating INVOKANA® 100 mg. Consider adding another antihyperglycemic agent in patients who require additional glycemic control.

- **Digoxin:** There was an increase in the AUC and mean peak drug concentration of digoxin when co-administered with INVOKANA® 300 mg. Monitor appropriately.

- **Positive Urine Glucose Test:** Monitoring glycemic control with urine glucose tests is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

- **Interference With 1,5-Anhydroglucitol (1,5-AG) Assay:** Monitoring glycemic control with 1,5-AG assay is not recommended in patients taking SGLT2 inhibitors. Use alternative methods to monitor glycemic control.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** INVOKANA® is not recommended in pregnant women, especially during the second and third trimesters.

- **Lactation:** INVOKANA® is not recommended while breastfeeding.
- **Pediatric Use:** Safety and effectiveness in patients <18 years of age have not been established.
- **Geriatric Use:** Patients ≥65 years had a higher incidence of adverse reactions related to reduced intravascular volume, particularly with the 300-mg dose; more prominent increase in the incidence was seen in patients who were ≥75 years. Smaller reductions in HbA1c relative to placebo were seen in patients ≥65 years.
- **Renal Impairment:** The efficacy and safety of INVOKANA® for glycemic control were evaluated in a trial that included patients with moderate renal impairment (eGFR 30 to <50 mL/min/1.73 $m^2$). These patients had less overall glycemic efficacy, and patients treated with 300 mg per day had increases in serum potassium, which were transient and similar by the end of the study. Patients with renal impairment using INVOKANA® for glycemic control may be more likely to experience hypotension and may be at a higher risk for acute kidney injury. INVOKANA® is contraindicated in patients with ESKD on dialysis.
- **Hepatic Impairment:** INVOKANA® has not been studied in patients with severe hepatic impairment and is not recommended in this population.

OVERDOSAGE

- In the event of an overdose, contact the Poison Control Center and employ the usual supportive measures.

ADVERSE REACTIONS

- The most common adverse reactions associated with INVOKANA® (5% or greater incidence) were female genital mycotic infections, urinary tract infections, and increased urination.

Please read the full Prescribing Information and Medication Guide available at www.Invokana.com/PI.

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**Dr Caudle:**
Well, that's a great way to round out our discussion for today. I'd like to thank Dr Gates Colbert for joining me today to discuss INVOKANA® and the treatment of diabetic nephropathy, or diabetic kidney disease, in patients with type 2 diabetes. Please read the full Prescribing Information and Medication Guide available at www.Invokana.com/PI.

Dr Colbert, thank you so much for being with us today.

**Dr Colbert:**
Yes, thank you Dr Caudle. It was a great discussion.

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