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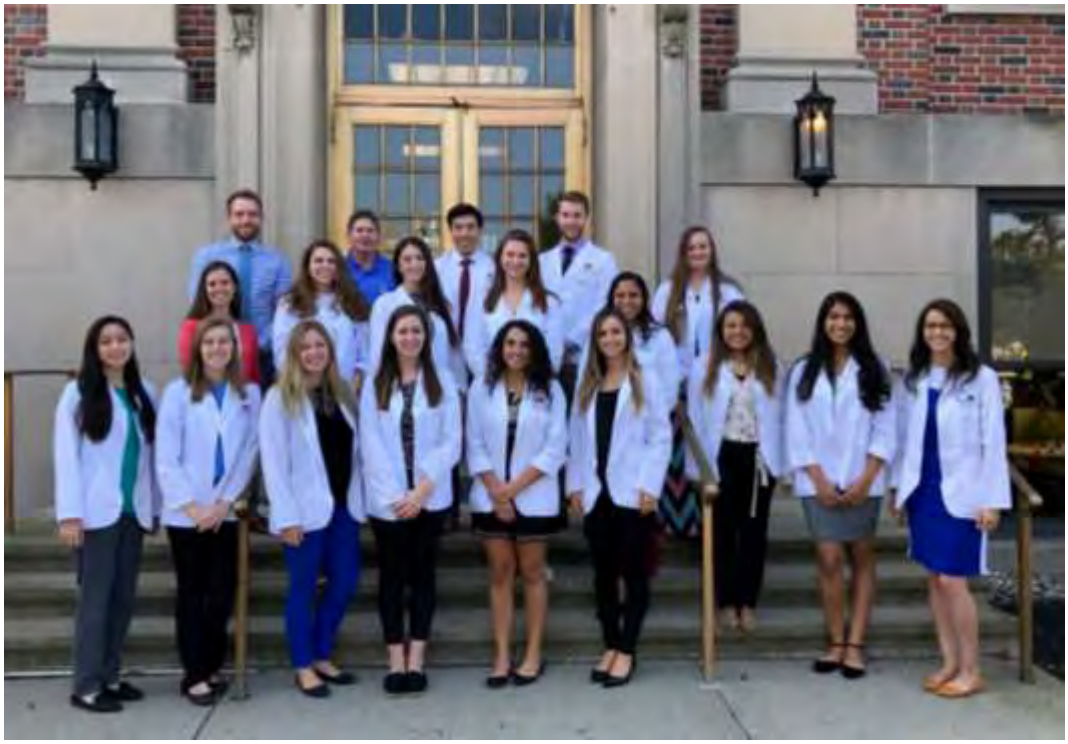

The Student Chapter of ACCP at Albany College of Pharmacy and Health Sciences is focused on preparing students who wish to take their education further with post-graduate training, faculty positions, or independent research positions. Our chapter promotes professionalism, leadership, and service. This is accomplished through direct patient care events focused on serving the underserved population in the Albany area. Our chapter currently has four patient care projects, one of which includes our Cardiovascular and Renal Disease (CaRE) screenings. This project works in collaboration with the Northeast Kidney Foundation to provide free health screenings to the public including blood pressure, cholesterol, blood glucose, and urinalysis testing followed by medication and lifestyle counseling. Students are given the opportunity to become certified in these trainings by attending a session to learn these skills prior to participating in these events.

A second patient care project our chapter has developed over the past couple of years is "CaRE for KIDneys" which focuses on teaching elementary and middle school students the importance of taking care of their health early on to prevent chronic disease in the future such as diabetes, hypertension, and chronic kidney disease. Our students educate the children through an interactive approach to get them excited to learn about their health. This includes games, true/false questions, and rewarding them with prizes. CaRE for KIDneys focuses on teaching kids a healthy lifestyle through diet and exercise to help them on a path to a healthy adult life.

Script your Future is another patient care project that focuses on the importance of medication adherence and preventative health. Our events focus on educating the public on why it is vital to adhere to their medications, and we discuss common barriers to not taking medications. We answer their questions on why they must take medications as directed and teach ways in which they can remember to take their medications. We also hand out pill boxes, wallet-sized medication cards, and tell the public about downloadable applications if they have a smart phone. Preventative health measures are also discussed including vaccination schedules and timing for health screenings.

Just this past semester our chapter has added a new patient care project, the Epilepsy Project. The goal of the Epilepsy Project is to raise awareness and provide support through education about epilepsy within the local community and our own college community. So far, the Epilepsy Project has held fundraising events where proceeds are donated to the Epilepsy Foundation of Northeastern New York. These include donations through Amazon, donation of clothing and household goods, and fundraisers at local restaurants. This project has also worked directly with the Northeast Epilepsy Foundation at events to raise awareness and educate the public on this disease.

Our chapter also holds three Clinical Pharmacy Challenge (CPC) nights each semester where students compete in teams of 3. Each night is a specific discipline, including: cardiovascular, self-care, infectious disease, endocrine, nephrology, neurology/psychiatry, and a mystery challenge each year that includes multiple topics. Student officers create questions based off of clinical guidelines, class materials, online resources, and textbooks. Faculty members who teach the individual courses review the questions and attend the challenges to facilitate questions that may arise. These challenges are completed through Turning Point ResponseWare, and multiple rounds with various types of questions are included. Prizes are awarded for 1st and 2nd place winners each night, and a grand prize winner is awarded at the end of each semester.

Our student chapter has grown immensely over the past couple of years with an increased number of events we have held throughout the community. Through our education, screenings, and preparation for further education, our ACCP student chapter is successfully preparing students for their future, all while serving underserved communities.

Maggie Sullivan, PharmD Candidate, ACPHS Class of 2019

Diabetes Medications and Cardiovascular Impact

Type 2 diabetes mellitus (T2DM) is a well-known risk factor for cardiovascular disease (CVD).[1] As a result, there is increased risk of mortality with the combination of diabetes and cardiovascular (CV) events. The preferred first-line anti-diabetic agent today is metformin because of its high efficacy, tolerability with appropriate dosing strategies, affordable cost, and beneficial outcomes.[2] In the UKPDS, metformin has demonstrated the ability to reduce CV mortality risk in patients with type 2 diabetes, particularly those who were overweight.[3] However, metformin alone is often not sufficient in many patients to achieve adequate glycemic control, especially in patients with long-standing or poorly controlled diabetes; as a result, add-on medications are often required. Until recently, there have been no prospective trials demonstrating ability to reduce CV outcomes with an anti-diabetic agent.

Medications that have published data demonstrating CV safety include a variety of medication classes. Two SGLT2 inhibitors including canagliflozin (Invokana) and empagliflozin (Jardiance) have beneficial CV effects in patients with T2DM. Canagliflozin's outcome study, CANVAS, enrolled patients with T2DM with high CV risk.[4] The primary outcome was a composite of death from CV causes, nonfatal myocardial infarction (MI), or non-fatal stroke. The rate of the primary outcome was lower with canagliflozin (26.9) than with placebo (31.5) per 1000 patient-years (hazard ratio, 0.86; 95% confidence interval, 0.75 to 0.97; P<0.001 for noninferiority; P=0.02 for superiority). Although canagliflozin reduced the primary composite endpoint, there were no significant drivers for the primary outcome. The EMPA-REG OUTCOME assessed the use of empagliflozin in patients with established CV disease and had the same primary outcome as CANVAS.[5] The primary outcome occurred in 10.5% of the empagliflozin group and 12.1% of the placebo group (hazard ratio, 0.86; 95.02% confidence interval, 0.74 to 0.99; P=0.04 for superiority. It may also reduce hospitalization due to heart failure and overall death rates. Advantages of these two medications include once daily oral administration, lowering A1c levels by 0.7-1.1%, decrease in both fasting plasma glucose (FPG) and post prandial glucose (PPG), weight loss, and lower blood pressure. Disadvantages include high cost and severe side effects such as risk of amputation, primarily at the level of the toe or metatarsal with canagliflozin, urinary tract infections, genital mycotic infection, hypotension, dehydration and acute kidney infection (AKI).

Liraglutide (Victoza), a GLP-1 receptor agonist, has published data that show CV benefit in patients with T2DM and either established cardiovascular disease (CVD) or high risk.[6] The primary outcome of this study was the first occurrence of death from CV causes, nonfatal MI or nonfatal stroke. The primary outcome occurred in significantly fewer patients in the liraglutide group (13%) compared to the placebo group (14.9%) (hazard ratio, 0.87; 95% confidence interval, 0.78 to 0.97; P<0.001 for noninferiority; P=0.01 for superiority). Advantages of liraglutide include an A1c lowering of 0.8-1.9%, weight loss, decrease in both FPG and PPG, and once daily dosing. Disadvantages include parenteral administration, GI adverse effects, and cost.

Lastly, pioglitazone (Actos) has CV outcome data that shows CV benefit in patients with insulin resistance based the homeostasis model assessment of insulin resistance (HOMA-IR) index and who had prior transient ischemic attack. The primary outcome of the IRIS trial was fatal or nonfatal stroke or MI.[7] It was determined that the primary outcome occurred in 9% of the pioglitazone group and 11.8% of placebo group (hazard ratio, 0.76; 95% confidence interval, 0.62 to 0.93; P=0.007). In addition to lowering the risk of stroke and MI, pioglitazone was also associated with lower risk of diabetes. Another study, PROactive, showed that use of pioglitazone for three years in patients with T2DM may reduce risk of all-cause mortality, non-fatal MI and stroke.[8] The primary outcome of this study was to evaluate stroke and other CV outcomes in patients with and without prior stroke. The results showed a benefit with pioglitazone for the primary end points including leg revascularization. When revascularization was taken out, the results were significant. Advantages of pioglitazone include A1c lowering of 0.8-1.5%, reductions in both FBG and PPG, low risk of hypoglycemia,

and use in renal disease. Disadvantages include a delayed onset of action and adverse effects such as weight gain, edema, congestive heart failure, and fractures.

Until 2008, CV outcomes data were not required by the United States Food and Drug Administration, but now any anti-diabetic agent coming to market has to demonstrate CV safety. Alpha-glucosidase inhibitors such as acarbose (Precose) currently have CV outcome data in Chinese patients with impaired fasting glucose and CV disease (Acarbose Cardiovascular Evaluation) but no benefit was found.[9] The amylin analog, pramlintide (SymlinPen), does not have data regarding CV impact. Linagliptin (Tradjenta), a DPP-4 inhibitor, does not currently have CV outcome data but the CAROLINA and CARMELINA studies in patients with T2DM are currently ongoing to assess CV mortality and morbidity.[10, 11] GLP-1 agonists, including albiglutide (HARMONY) [12], and dulaglutide (REWIND), [13] do not have outcome data but each have their own respective ongoing trials to assess CV impact. Other medications such as nateglinide (NAVIGATOR) [14] and dapagliflozin (DECLARE-TIMI58)[15] also do not have outcome data and are either complete or are undergoing studies to assess their CV outcome data.

In conclusion, metformin is currently the recommended first-line agent used to treat T2DM. In patients requiring add-on medications, SGTL2 inhibitors should be considered, as each have data demonstrating CV benefit (CANVAS and EMPA-REG OUTCOME trials). In addition to improving glycemic control, SGTL2 inhibitors also lower blood pressure and are associated with modest weight loss. However, there have been higher incidences of side effects such as UTIs, yeast infections and AKI with this class of medication. In patients using canagliflozin, there have been reports of toe and mid-foot amputations; therefore, prescribers should be cognizant of the aforementioned risk factors when prescribing canagliflozin and may consider empagliflozin instead. Liraglutide may also be considered for patients with T2DM and high CV risk because it decreases CV death and mortality (LEADER trial). The advantages and disadvantages associated with each class of anti-diabetic medications should be considered on a case-by-case basis, incorporating both perceived risks and benefits with a given therapy.

Medication	**Hazard Ratio**	**95% Confidence Interval**	**P-value**
Canagliflozin (Invokana)	0.86	0.75 to 0.97	P<0.001 for noninferiority P<0.02 for superiority
Empagliflozin (Jardiance)	0.86	0.74 to 0.99	P<0.001 for noninferiority P=0.04 for superiority
Liraglutide (Victoza)	0.87	0.78 to 0.97	P<0.001 for noninferiority P=0.01 for superiority
Pioglitazone (Actos)	0.76	0.62 to 0.93	P=0.007

Table 1. Data Summary

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Gavin Leung, PharmD Candidate, ACPHS Class of 2019

Clinical Spotlight: John Faragon, PharmD

Pharmacist at Albany Medical Center and the Regional Pharmacy Director for the Northeast Caribbean AIDS Education and Training Center (AETC)

What are your daily main roles and responsibilities in your current position?
"I work with the Division of HIV Medicine and round most days of the week on our inpatient population who are receiving care for a variety of medical issues, some HIV-related and some are not."

Has there been anyone that you've met throughout your career who may have influenced or helped you get to where you are today?
"I think back to my days at ACPHS and there were a number of clinical faculty that encouraged many of us to obtain additional training either through the Doctor of Pharmacy degree (remember, most of us graduated with a BS Degree) or through residency training. One person I recall is Dr. Bobby Bryant who ran the pediatric elective with Tom Lombardi. I recall he asked me one day if I was going to get my PharmD and I really wasn't planning on it – I remember he said to me in his

southern drawl, 'John, You just have to go back and get your PharmD,' and I think that was what I always remembered when I went back to school."

What advice would you give to a pharmacy student who is interested in pursuing a career in clinical pharmacy?
"Do a residency, then do another one, then do a fellowship if it's available. Residency training will be critical to success in the clinical pharmacy field in the future."

How do you see your role as a clinical pharmacy specialist evolving over the upcoming years?
"I think as HIV has changed, our role in these positions has also changed. We used to have 15-20 patients on service; now the service sometimes dips down to 5-7 patients. Our role is even more crucial as we admit our patients to the hospitalist service, often with many complex medical issues, and as our patients get older, they are more prone to diabetes, cardiovascular disease, cancer, liver disease, and renal issues. My role, while still specializing in HIV, has changed to include understanding and predicting drug interactions with primary care medications; that has been even more valuable to our providers than the HIV piece. Also, the explosion of HCV treatments and their complexities has changed a lot of what we do. In the future, these complexities will only become more difficult to manage and I see our role continuing to evolve."

Have there been any roadblocks in your pharmacy career? And if so, how did you overcome them?
"The most important roadblock I can think of is when you are young and thinking you know everything. When dealing with prescribers, try to give options, not just one answer; leave it to the physician to make the final choice of therapy. When you come across as someone who is providing options, I think you are more appreciated and respected, rather than coming off as a "know it all." Also, when you are young, just say, 'I don't know, I'll have to look it up,' if you in fact do not know a given answer. This will only help you gain credibility with the providers you work with on a regular basis."

As an HIV specialist, what advice would you give to other pharmacists and interns on how to stay up to date and educated in the area and how they can provide the best care to their patients?
"Read every day – something – related to your disease specialty. Even if it's a summary of a topic related to your disease state, it's the only way to keep up. Be sure to read as much as you can, especially when you are young. Also find a good physician mentor to do research alongside of. I had Peter Piliero and Doug Fish years ago – they did wonders for my career and future opportunities and I continue to be grateful to them."

Finnella Morgan, PharmD Candidate, ACPHS Class of 2019

Betrixaban for Venous Thromboembolism (VTE) Prophylaxis in the Acute Medically Ill

Direct oral anticoagulants (DOACs) were developed to target specific factors in the coagulation cascade to improve patient outcomes and reduce complications associated with non-specific anticoagulants, such as vitamin K antagonists and heparin. The success of the current DOACs comprised of dabigatran, rivaroxaban, apixaban and edoxaban drove the development of a drug tailored towards an area of unmet clinical need. Betrixaban (BEVYXXA®) is a new factor Xa inhibitor that will be joining the family of DOACs with specific use in acute medically ill patients. It is the first in its class to be approved for extended venous thromboembolism (VTE) prophylaxis in acute medically ill patients[1]. It was approved by the FDA on June 23, 2017 for prophylaxis of VTE in adult patients hospitalized for an acute medical illness who are at risk for thromboembolic complications due to moderately or severely restricted mobility and other risk factors for VTE[2]. The approval of betrixaban was based on the Portola Pharmaceuticals' pivotal trial, APEX. The Acute

Medically Ill VTE Prevention with Extended Duration Betrixaban (APEX) trial, completed in January of 2016, was a randomized, double-blind, double-dummy, active-controlled multinational clinical trial that compared subcutaneous enoxaparin and oral betrixaban[3]. Enoxaparin was dosed at 40 mg once daily for 10 ± 4 days plus oral placebo for 35 to 42 days and oral betrixaban was dosed at a loading dose of 160 mg on day 1 and 80 mg once daily for 35 to 42 days plus subcutaneous placebo for 10 ± 4 days. Patients with severe renal insufficiency (CrCl ≥ 15 to < 30 mL/minute) or on concomitant P-gp inhibitors received 50% of the pre-specified dose of each study medication. The overall study population was broken into three cohorts based on D-dimer level and age. Cohort 1 included patients who had an elevated baseline D-dimer level, cohort 2 included patients in cohort 1 plus those who were 75 years of age and older and cohort 3 included the overall study population. The decision to test trial outcomes in these subgroups was based on the expectation that patients with an elevated D-dimer level or an age of at least 75 would represent a subgroup with both a greater risk of VTE and a greater benefit of extended duration antithrombotic therapy[3]. Statistical significance for cohort 1 was not met, therefore all subsequent efficacy outcomes were considered to be exploratory and were not used to draw conclusions regarding statistical significance. The trial met its primary efficacy outcome and concluded fewer events of asymptomatic or symptomatic proximal VTE, non-fatal pulmonary embolism, or VTE-related death. The major safety outcome, occurrence of major bleeding, was 0.6% in the betrixaban group and 0.7% in the enoxaparin group. The net clinical benefit, comprised of the primary efficacy outcome and the principle safety outcome, was 5.8% in the betrixaban group and 7.3% in the enoxaparin group.

To ensure competitive edge over the current approved DOACs, the clinical development of betrixaban was targeted towards a population lacking safe and efficacious therapy[4]. Aside from betrixaban being the only DOAC approved for its indication, its favorable pharmacokinetic characteristics offer a potential advantage over others in its class. Betrixaban has the least renal clearance, with approximately 11% renal excretion of the orally administered dose[4]. This pharmacokinetic characteristic is extremely favorable since betrixaban can be used in patients with severe renal impairment. A 50% dose reduction is necessary in patients with renal insufficiency. In addition, less than 1% of betrixaban is hepatically metabolized. Therefore, this DOAC has minimal drug-drug interactions related to CYP450. Betrixaban is a substrate for P-gp. Concomitant use of betrixaban with P-gp inhibitors results in increased exposure of the drug. A 50% dose reduction is necessary for patients starting concomitant P-gp inhibitors. The majority of this drug is excreted via the feces. Betrixaban can be administered once daily because it has a half-life of approximately 20 hours. Although once daily dosing is appealing to patients, it has raised concerns due to the nature of the medication. An anticoagulant with a 20-hour half-life and no antidote can complicate the management of patients who may experience life-threatening bleeding or those who require emergency surgery. The risk of bleeding is apparent with all anticoagulants, therefore all patients taking this class of medication should be aware of the signs and symptoms of bleeding.

All things considered, betrixaban displays appealing characteristics and a high potential for clinical use in acute medically ill patients. In the United States, acutely ill medical patients account for more than 20% of the attributable risk for VTE [3]. According to a retrospective study on the use of thromboprophylaxis in patients who subsequently developed a VTE after hospital discharge, patients are hypercoagulable up to 90 days' post discharge and are at a higher risk for developing VTE[5]. The extension of treatment with oral betrixaban after hospital discharge may reduce VTE among specific patients and prevent readmissions by providing a longer duration of thromboprophylaxis. Its role in practice can provide patients with extended prophylaxis post discharge, with no greater risk in major bleeding compared to standard duration enoxaparin. Further studies should be performed to determine if a larger role for this drug exists in the management of VTE as well as stroke prevention.

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Jenna Ciervo, PharmD Candidate, ACPHS Class of 2019

MiniMed 670G: The First FDA Approved Hybrid Closed-Loop Insulin Delivery System

Fulfilling its mission of "contribution to human welfare by the application of biomedical engineering," Medtronic's MiniMed recently released the MiniMed 670G Insulin Pump system, the first hybrid closed-loop insulin delivery system (insulin pump and continuous glucose sensor) on the market. The system, indicated for use in type 1 diabetes patients age 14 years or greater, includes a continuous glucose monitor (CGM) system that communicates with the insulin pump and uses an algorithm to automatically adjust basal insulin delivery and suggest bolus insulin delivery or termination.

While the insulin pump and continuous glucose monitors are not new in the world of diabetes, they have not previously been linked to work interdependently, freeing the patient from some responsibilities of the disease. In the hybrid closed-loop system, the calibrated continuous glucose monitor feeds interstitial glucose levels to the insulin pump every five minutes. Type one diabetes patients utilizing this system must still account for carbohydrate intake and administer bolus doses of insulin for meals, however the CGM will continually monitor their blood glucose levels, and automatically link these levels to the pump. The insulin pump is then able to suggest bolus insulin rates (according to ratio calculations from an endocrinologist) as the blood sugar rises.[1] This means less finger pricks and undetected high blood sugars.

Prior to this linked technology, patients utilizing an insulin pump would have to manually input their blood glucose levels prior to administering insulin. Their blood glucose levels could be obtained from blood glucose monitors that require a blood sample, or from a continuous glucose monitor that is constantly worn and receiving constant blood glucose readings.

The MiniMed670G insulin pump is linked to the Guardian Sensor 3 glucose monitor and transmitter. The sensor requires calibration with a glucose monitor twice a day. During trials, subjects of Medtronic were provided with the same monitor, a Contour Next Link glucose meter, to ensure consistency.[4] The Guardian continuous glucose monitor linked in this hybrid-closed loop system is the first CGM to be FDA approved for bolus doses[3], which means patients are able to administer a bolus of insulin according to the CGM blood glucose reading, provided proper calibration has been completed. During this three month study there were no episodes of diabetic ketoacidosis or severe hypoglycemia reported, and subjects experienced a 0.5% decrease in HbA1C.[5]

The MiniMed 670G also includes two personalized features; suspend before low, and auto mode. In suspend before low, a predetermined low blood sugar reading is set into the pump. If the patient begins to approach these limits, insulin delivery will be suspended for 30 minutes. In auto mode, basal delivery rates will adjust every five minutes as needed according to glucose levels determined by the CGM device. This new technology has the potential to make life much easier for people with type 1 diabetes. The technology has been listed as Time Magazine's best 25 inventions of 2016, and the Juvenile Diabetes Research Foundation calls it 'A life-changing breakthrough."[3]

While the device does allow for a simpler and more stream-lined process of correcting blood glucose levels, the responsibility of utilizing the technology to full potential still remains in the hands of the patient. The patient may be alarmed of blood glucose changes, however the pump still requires manual bolus administration, and the continuous glucose monitor requires consistent and accurate calibration twice daily. The device has the potential to streamline the maintenance of diabetes care, but management by the patient is imperative.

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Madyson Allard, PharmD Candidate, ACPHS Class of 2020

CANVAS Study

Type 2 diabetes is a disease that 9 per 100 people nationally are diagnosed with each year.[1] Within patients diagnosed with type 2 diabetes there is an estimated 90,950 deaths attributed to cardiovascular disease and 33,002 deaths attributed to end stage renal disease per year[1]. Type 2 diabetes is typically considered a risk equivalent for cardiovascular disease, especially with other known cardiovascular risk factors and the leading cause for end-stage renal disease.[1] Mechanistically, sodium-glucose cotransporter-2 inhibitors (SGLT2) target the kidneys and lower the renal threshold for glucose excretion.[2] In practice, SGLT2 inhibitors are used as an adjunct therapy with diet, exercise, and possibly other medications to improve glycemic control.[2] Prior to available outcomes data, this class of medication was not only associated with improved glycemic control, but modest reductions in both blood pressure and weight. Two years ago, SGLT2 inhibitor, empiglaflozin, was studied. CV outcomes were also assessed in the Cardiovascular Assessment Study (CANVAS program) which was found to have positive cardiovascular and renal outcomes.[3]

In July 2017, results from canagliflozin's outcome study, CANVAS, a randomized, international, double-blinded, placebo-controlled study were released. Key inclusion criteria were as follows: type 2 diabetes mellitus with an A1C 7% ≤ A1C ≤ 10.5%, eGFR greater than 30 mL/min/1.73 m^2, 30 years of age or older with symptomatic atherosclerotic cardiovascular disease or ≥ 50 years old with at least 2 CV factors (diabetes duration ≥10 years, SBP > 140 mmHg on ≥ 1 antihypertensive medication, current smoker, micro- or microalbuminuria, or HDL cholesterol <39mg/dL.).[3] Note, unlike the EMPA-REG outcome, which included only secondary prevention subjects, CANVAS enrolled both primary and secondary prevention cohorts. Within

CANVAS, the data from two trials were integrated resulting in a total of 10,142 participants with type 2 diabetes and high cardiovascular risk. Participants in each trial were randomly assigned to receive canagliflozin 100 or 300 mg or placebo, in addition to their insulin regimen and were followed for a mean of 188.2 weeks.[3] Background anti-diabetic therapy primarily consisted of metformin, sulfonylurea and/or insulin. Cardioprotective therapies (e.g., statins, renin-angiotensin-aldosterone system [RAAS] inhibitors, etc.) were prevalent at baseline[3]. In addition, there was pre-specified sequential testing for additional endpoints. Of note, the CANVAS Program actually included two sub-studies, CANVAS and CANVAS-R; data from CANVAS were electively unblinded by the sponsor over a class concern about elevated low-density lipoprotein cholesterol and unknown cardiovascular implications. Thereafter, the sponsor elected to initiate another trial with the same inclusion/exclusion criteria[3].

The primary major adverse cardiovascular endpoint (MACE) in CANVAS was death from cardiovascular causes, nonfatal myocardial infarction, and nonfatal stroke.[3] The primary MACE outcome was assessed based on the intent-to-treat principle with 90% power; if non-inferiority was met, the study could assess for the superiority of canagliflozin for the primary MACE endpoint.[3]

The hazard ratio for the primary MACE outcome was 0.86; canagliflozin was found to be superior to placebo (p-value < 0.001 for non-inferiority; $p = 0.02$ for superiority). However, the MACE endpoint was not driven by a particular CV endpoint. Not only did this study show positive outlook toward cardiovascular events but potentially renal benefits, too. However, as all-cause mortality was not found to be significant, these findings should be interpreted as only exploratory;[3] future renal outcomes studies are underway (e.g., CREDENCE). Despite observed benefits there was an increased risk of fracture, and an emergent increased adverse effect of amputation.[2,3]

Are these results significant? Yes! The findings from the CANVAS Program have significant implications; the CANVAS Program results further suggest a class effect in a high-risk cohort at reducing CV events beyond glucose-lowering effects.[3] Type 2 diabetes is a well-recognized risk factor, if not risk equivalent for CV disease and the leading cause for patients requiring dialysis.[1] To further reduce a patient's residual risk, this class of medications should be considered, in addition to known cardioprotective agents (e.g., statins, RAAS inhibitors, etc.). This can be great evidence to help change practice and give additional options and therapy for patients already on an ACEi/ ARB but still need more aggressive treatment to provide patients with increased morbidity/mortality benefit as well as prevent comorbidities seen to develop with type 2 diabetes. However, one has to balance the known risks of therapy, which now includes amputations, with the perceived benefits of therapy.

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2. INVOKANA® [prescribing information]. Titusville, NJ: Janssen Pharmaceuticals, Inc. 2017
3. Bruce Neal, M.B., Ch.B., Ph.D., Vlado Perkovic, M.B., B.S., Ph.D., Kenneth W. Mahaffey, M.D., et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J August 2017; 377:644-657.

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