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An independent chapter of the American College of Clinical Pharmacy, the DC-CCP is dedicated to improvements in pharmacotherapy practice, education, and research in the District of Columbia, Maryland, and the Commonwealth of Virginia.

PRESIDENT'S LETTER

It is hard to believe that 2017 is quickly coming to an end. We have been busy at DC-CCP with many member networking events, residency preparation events for our students, and a successful Fall CE Event!

The Fall CE Event was hosted by Holy Cross Hospital and featured clinical pharmacist presenters from University of Maryland Medical Center and Johns Hopkins Hospital. Topics included identification and treatment of ICU delirium, medication error prevention, and special considerations for blood pressure management in elderly patients. Students and residency program directors also participated in a roundtable networking session. It was a great opportunity to catch up with some friends and colleagues and to meet some new members.

Our student and resident networking & education committee has hosted a number of events to help students navigate the residency application process. The mentorship program is also launching, which offers an opportunity for students and residents to meet and learn from each other. Meanwhile, our pharmacist networking & education committee hosted a fun outing to a National's game.

As the year wraps up, I want to thank all of the students, residents and pharmacists who have made these DC-CCP events a success!

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DC-CCP MEMBER SPOTLIGHT:

SEAN T. LASOTA, PHARMD, BCACP

Interviewed by: Angeo Rey Belen, 3rd Year Student Pharmacist, University of Maryland School of Pharmacy

In the world of ambulatory care pharmacy, every day is a little different, but it's always exciting. That's certainly the case for Sean T. Lasota, PharmD, BCACP, a clinical ambulatory care pharmacist. To Dr. Lasota, his specialty is focused on providing integrated patient care, especially to those with chronic conditions, in a variety of outpatient settings. Dr. Lasota prefers providing comprehensive care and interacting with patients directly, and ambulatory care has given him the opportunity to have these experiences with the latitude to be independent but also be part of a team. His days involve triaging questions, serving as a resource to primary care physicians, and seeing patients whether they are scheduled or walk-ins. While patients with diabetes, hypertension, or hyperlipidemia are common for ambulatory care practitioners, his unique position at Kimbrough Ambulatory Care Center and its ties to military personnel allow him to also see behavioral health patients regularly. That is why to him, an ideal ambulatory care pharmacist has the ability to understand the patient holistically while also maintaining an empathic nature to build and maintain strong rapports over a long period of time. In fact, he finds it especially satisfying to tell a patient they are at goal: that thanks to all the patient's hard work and dedication, their health problem is now better controlled.

Originally from New Jersey, Dr. Lasota's pharmacy experiences have taken him to many locations. While attending Philadelphia College of Pharmacy (now the University of the Sciences in Philadelphia), his internal medicine advanced pharmacy practice experience (APPE) rotation gave him an opportunity to see what clinical pharmacists do and how they use their clinical acumen every day to help patients. Ultimately, this would spur him to pursue clinical pharmacy. After receiving his PharmD degree, Dr. Lasota completed a PGY-1 residency in Community Pharmacy at Duquesne University and Giant Eagle Pharmacy. He then went on to the University of Saint Joseph where he served as Assistant Professor of Pharmacy Practice. Afterwards, he went on to the Johns Hopkins Hospital where he served as Clinical Coordinator and completed his PGY-2 residency in ambulatory care. Then in September 2017, he moved to his current position at Kimbrough Ambulatory Care Center. Currently, Dr. Lasota is involved with ACCP, ASHP, and DCCCP. Throughout all his experiences, Dr. Lasota believes his most significant one (outside of getting married) was being able to graduate with a doctorate and move up in the field of pharmacy while helping others along the way. Looking towards the future, Dr. Lasota hopes to become more involved with research publications, pharmacy organizations, and academia. In the meantime, he's enjoying reading, cooking, traveling, and spending time with his friends and family. If he weren't a pharmacist, Dr. Lasota believes he would be a science teacher or college professor as he thoroughly enjoys the academic environment and the moment when the lightbulb turns on in someone's head. For students, his best advice is to reach out to your professors and see what they do. If you do not know about a pharmacy field, you won't know what it is about until you see or experience it.

His current guiding philosophy is to "try and be a good person then let things work out the way they do. Everyone has their ups and downs, but if you try to be a good person, help others, and do your best, did you really go wrong?" Dr. Lasota has made great strides in his career, and as he continues his clinical journey, undoubtedly this philosophy will push him towards even greater success.

HIGHLIGHTING GERIATRIC PHARMACY:

INTERVIEW WITH NICOLE BRANDT, PHARMD, MBA, BCPP, BCGP, FASCP

Interviewed by: Masomeh Saleh, 3rd Year Student Pharmacist, University of Maryland – School of Pharmacy

Dr. Nicole Brandt is a trail blazer in the world of geriatric pharmacy. After having been a professor at the University of Maryland in Baltimore (UMB) School of Pharmacy for more than a decade, she has enhanced her career by taking on additional roles. More recent responsibilities include becoming the Executive Director of the Peter Lamy Center on Drug Therapy and Aging at the UMB School of Pharmacy in addition to leading the implementation of pharmacist directed services within the Center for Successful Aging at MedStar Good Samaritan Hospital.

Dr. Brandt's career in pharmacy began in her cousin's independently owned community pharmacy when she was just 15 years old. She did third party billing for the pharmacy, but quickly grew to love the interaction between the pharmacist and the patients. She obtained her PharmD degree from the UMB School of Pharmacy and it was during her 4th year rotation that she realized her passion for geriatrics. She always had a strong relationship with her grandparents and really enjoyed giving back to a generation that had given so much to her. As a result, Dr. Brandt continued at UMB and completed a one year General Pharmacy residency with a focus in geriatrics.

Dr. Brandt has always enjoyed having a broader impact on health care. She loves direct patient care especially with the older adult population, but also enjoys advocating for policies that can improve patient care. She knew healthcare was becoming more of a business, especially with the changing healthcare climate, so she decided to obtain an MBA in healthcare management from University of Baltimore/Towson University. The MBA gave her a new perspective and the ability to influence future healthcare services. In addition to her MBA, Dr. Brandt holds Board Certifications in Geriatric and Psychiatric Pharmacy. She is an active member of the American Society of Consultant Pharmacists (ASCP) and just completed her 3-year tenure as President-Elect, President, and Chairman of the Board. She hopes to create more innovative models of care while keeping them as patient centered as possible. Dr. Brandt believes we could utilize our health care resources more wisely, especially since geriatrics is becoming more of a focus.

Finally, even though her time is divided between her incredibly demanding clinical and academic responsibilities, she still manages to enjoy time with her family in addition to completing triathlons and baking.

QUARTER-DOSE THERAPY FOR THE TREATMENT OF HYPERTENSION

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The National Health and Nutrition Examination Survey estimates that about 30% of United States adults have hypertension, the leading reason for adult clinician visits in the United States.[1] Despite its prevalence in this country and the fact that hypertension is the most common cause of morbidity and mortality worldwide, only about one third of patients receiving pharmacologic treatment achieve blood pressure control.[2] Current JNC 8 guidelines recommend a goal of <140/90 mmHg for patients under the age of 60 and all patients with diabetes or CKD, and a goal of <150/90 mmHg for patients age 60 or older.[3] In many cases, therapy with more than one agent is required in order to reach these blood pressure targets.[4]

A recent meta-analysis by Bennett et al. examined literature comparing quarter-doses of antihypertensive agents to placebo and standard-dose monotherapy. This systematic review included 38 studies reporting quarter-dose monotherapy, 7 studies reporting dual quarter-dose therapy, and 2 reporting quadruple quarter-dose therapy. Table 1 displays all of the standard doses used in this review as well as corresponding quarter-doses, although many of them are not often seen in practice in the US. Compared to placebo, single-agent quarter-dose therapy led to a -4.7/-2.4 mmHg (95% CI, -5.4 to -3.9/-2.8 to -1.9, *P*<0.001) decrease in blood pressure with consistency across all 5 drug classes. Patients achieved an average decrease of -6.7/-4.4 mmHg (95% CI, -8.6 to -4.8/-5.5 to -3.3, *P*<0.001) with two quarter-dose agents, and a decrease of -22.4/-13.1 mmHg (95% CI, -28.3 to -16.5/-17.3 to -8.8, *P*<0.001) with four quarter-dose agents. When compared to standard-dose monotherapy, single agent quarter-dose therapy was less efficacious by 3.7/2.6 mmHg (95% CI, 3.0-4.5/2.2-3.1, *P*<0.001). However, there was no significant difference between dual quarter-dose therapy and standard-dose monotherapy (+1.3/-0.3 mmHg), and a blood pressure decrease of -13.1/-7.9 mmHg (95% CI, -20.1 to -6.1/-12.1 to -3.7, *P*<0.001) with quadruple quarter-dose therapy compared to standard-dose monotherapy.[5]

Researchers found no significant difference in the risk of adverse events in any single-agent (RR=1.0 [0.91-1.2]), dual-agent (RR=0.93 [0.29-2.9]), or quadruple-agent (RR=2.0 [0.2-20.2]) regimen compared to placebo. In addition, there were significantly fewer reported adverse events in the single and dual quarter-dose therapy regimens compared to standard-dose monotherapy. Of the 8 studies that reported potassium concentrations, there were no significant differences when compared to placebo, but standard-dose thiazide monotherapy led to a significantly greater decrease in serum potassium than quarter-dose thiazide therapy (-0.27, 95% CI, 0.08-0.45 mEq/L, *P*=0.01). Quadruple quarter-dose therapy led to small increases in both uric acid (0.03, 95% CI, 0.001–0.04 mmol/L; *P*=0.003) and serum creatinine (4.4, 95% CI, 0.9–7.8 mmol/L; P=0.02), compared to placebo.[5]

This report suggests that dual quarter-dose therapy has comparable blood pressure-lowering efficacy to standard-dose monotherapy with fewer adverse effects. As hypertension itself is often asymptomatic, it is important to minimize treatment-related side effects to avoid encouraging nonadherence. To do so, it may be prudent to consider quarter-dose rather than standard-dose therapy. However, it is important to note that quarter-doses are not manufactured for all medications and may require patients to split tablets on their own. Ease of use

considerations, pill burden, and additional copays associated with using multiple quarter-dose medications (if not coformulated) rather than standard-dose monotherapy are specific factors that must be considered when optimizing each patient's regimen. Further research should be conducted on this topic, especially because data surrounding quarter-dose regimens with more than two medications is sparse.

Table 1: Standard and Quarter-Doses of Antihypertensive Agents[5]

Medication	Standard-Dose (mg)	Quarter-Dose (mg)
Beta Blockers		
Atenolol	50	12.5
Bisoprolol	10	2.5
Carvedilol	25	6.25
Metoprolol	100	25
Nebivolol	5	1.25
Penbutolol	40	10
Calcium Channel Blockers*		
Amlodipine	5	1.25
Lercanidipine	10	2.5
Nitrendipine	20	5
Verapamil	240	60
ACE Inhibitors*		
Benazepril	20	5
Captopril	100	25
Enalapril	20	5
Fosinopril	10	2.5
Lisinopril	20	5
Quinapril	20	5
Trandolapril	2	0.5
Angiotensin Receptor Blockers*		
Azilsartan	40	10
Candesartan	8	2
Irbesartan	150	37.5
Olmesartan	20	5
Telmisartan	40	10
Valsartan	80	20
Thiazides*		
Bendroflumethiazide	2.5	0.625
Hydrochlorothiazide	25	6.25

*denotes typical first line class for the treatment of hypertension in the absence of CHF/MI

References
1. Egan BM, Zhao Y, Axon RN. US trends in prevalence, awareness, treatment, and control of hypertension, 1988-2008. *JAMA*. 2010;303:2043-2050.
2. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2224–2260.
3. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA*. 2014;311:507-520.
4. Gradman AH. Rationale for triple-combination therapy for management of high blood pressure. *J Clin Hypertens*. 2010;12:869–887.
5. Bennett A, Chow CK, Chou M, et al. Efficacy and Safety of Quarter-Dose Blood Pressure–Lowering Agents: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Hypertension*. 2017;70:85-93.

SGLT-2 INHIBITORS AND CARDIOVASCULAR OUTCOMES IN TYPE 2 DIABETES

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Reviewed by: Jessica Merrey, PharmD, MBA, BCPS, BCACP, BCGP, Clinical Pharmacy Specialist, The Johns Hopkins Hospital

As cardiovascular (CV) mortality is the leading cause of death in patients with type 2 diabetes, clinical interventions must address CV risk factors in addition to reduction in plasma glucose levels.[1] In 2013, the first sodium glucose cotransporter-2 (SGLT-2) inhibitor was FDA-approved for use, along with diet and exercise, to lower blood glucose in adults with Type 2 diabetes.[2] Currently, there are three FDA-approved SGLT-2 inhibitors: canagliflozin (Invokana®), empagliflozin (Jardiance®), and dapagliflozin (Farxiga®).[2] Inhibiting the SGLT-2 enzyme, which is responsible for renal absorption of filtered glucose, results in less filtered glucose reabsorption, thereby increasing glucose urinary excretion.[3] In addition to lowering plasma glucose concentration, the unique mechanism of action of SLGT-2 inhibitors allows for modulation of metabolic and hemodynamic effects that increase the risk of CV outcomes.[1, 4] Potential metabolic effects include HbA1c reduction; weight loss; increased fat oxidation; changes in plasma electrolyte concentrations; and increases in plasma ketone, uric acid, and glucagon concentrations. Possible hemodynamic effects include decreases in blood pressure, diuretic effects and a decrease in extracellular fluid volume, impaired arterial elasticity, and decreased sympathetic tone.[1]

EMPA-REG OUTCOME was the first trial to examine the effects of SGLT-2 inhibitors on CV outcomes in patients with Type 2 diabetes. This was a randomized, double-blind, placebo-controlled trial to determine the effect of empagliflozin versus placebo on cardiovascular events in adults with Type 2 diabetes. Subjects received empagliflozin 10 mg, empagliflozin 25 mg, or placebo once daily. The primary outcome was a composite outcome of death from cardiovascular causes, nonfatal myocardial infarction (MI) or nonfatal stroke.[5]

CANVAS combined data from two randomized, double-blind, placebo controlled trials that investigated the effects of canagliflozin on cardiovascular, renal, and safety outcomes. Patients received canagliflozin 100 mg or 300 mg daily or matching placebo. The primary outcome was a composite of death from cardiovascular outcomes, nonfatal MI, or nonfatal stroke.[6]

DECLARE-TIMI58 is an ongoing trial that is seeking to evaluate the impact of adding dapagliflozin to current DM therapy on MI, ischemic stroke, and CV death.[7] It has an estimated completion date of April 2019.

Please see the table below for a summary of the results.

Drug	Cardiovascular Outcome	Cardiovascular Outcomes Data
Empagliflozin	Improves	The primary outcome was reached in a lower percentage of subjects in the empagliflozin group than in the placebo arm (10.5% vs. 12.1%). The empagliflozin group had lower rates of death from cardiovascular causes (3.7%, vs. 5.9% in the placebo group; 38% relative risk reduction), hospitalization for heart failure (2.7% and 4.1%, in the placebo arm; 35% relative risk reduction), and death from any cause (5.7% and 8.3% in the placebo group; 32% relative risk reduction). Rates of strokes and MIs were similar between the empagliflozin and placebo groups.
Canagliflozin	Improves	The primary outcome was lower with canagliflozin than with placebo (26.9 vs. 31.5 participants per 1000 patient-years; hazard ratio, 0.86; 95% confidence interval [CI], 0.75- 0.97; P<0.001 for noninferiority; P=0.02 for superiority). Patients who received canagliflozin progressed to albuminuria less frequently than those who received placebo (89.4 vs. 128.7 subjects with an event per 1000 patient-years; hazard ratio of 0.73; 95% CI, 0.67- 0.79). Serious adverse events occurred less frequently in the canagliflozin than the placebo group (104.3 vs. 120.0 patients with an event per 1000 patient-years; hazard ratio, 0.93; 95% CI, 0.87-1.0), except for amputation (6.3 vs. 4.3 patients with an event per 1000 patient-years; hazard ratio, 1.97; 95% CI, 1.41-2.75).
Dapagliflozin	Currently being studied in the DECLARE-TIMI58 trial	

In conclusion, based on the results from the EMPA-REG OUTCOME and CANVAS trials, empagliflozin and canagliflozin reduce the risk of all-cause cardiovascular outcomes and death from any cause in patients with Type 2 diabetes. SGLT-2 inhibitors now have an FDA indication for cardiovascular protection in diabetic patients at an increased risk.

References

1. Abdul-Ghani M, Prato SD, Chilton R, Defronzo RA. SGLT2 Inhibitors and Cardiovascular Risk: Lessons Learned From the EMPA-REG OUTCOME Study. *Diabetes Care*. 2016;39(5):717-725.
2. Center for Drug Evaluation and Research. Drug Safety and Availability - FDA Drug Safety Communication: FDA revises labels of SGLT2 inhibitors for diabetes to include warnings about too much acid in the blood and serious urinary tract infections. U S Food and Drug Administration Home Page. https://www.fda.gov/Drugs/DrugSafety/ucm475463.htm. Accessed July 12, 2017.
3. DRUGDEX System [Internet]. Greenwood Village, Colorado: Thomson Reuters (Healthcare) Inc. 1974 [cited 2017 Jul 1
4. Inzucchi SE, Zinman B, Wanner C, et al. SGLT-2 inhibitors and cardiovascular risk: Proposed pathways and review of ongoing outcome trials. *Diabetes and Vascular Disease Research*. 2015;12(2):90-100
5. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T,

Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26; 373(22):2117-28
6. Neal B, Perkovic V, Mahaffey KW, Zeeuw DD, Fulcher G, Erondu N, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. New England Journal of Medicine. 2017 Dec
7. AstraZeneca. Bristol-Myers Squibb. The TIMI Study Group. Hadassah Medical Organization. ClinicalTrials.gov [Internet] Bethesda, MD: National Library of Medicine (US); 2000. [Accessed July 12, 2017]. Multicenter trial to evaluate the effect of dapagliflozin on the incidence of cardiovascular events (DECLARE-TIMI58) [cited 2017 Jul 10]. Available from:https://clinicaltrials.gov/ct2/show/NCT01730534?term=declare+timi+58&rank=1. NLM identifier: NCT01730534.

CANAGLIFLOZIN: NEW DATA, NEW BENEFIT, AND NEW RISK

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In 2013, canagliflozin (Invokana®) was the first FDA-approved sodium-glucose cotransporter 2 (SGLT2) inhibitor for the treatment of patients with type 2 diabetes mellitus.[1] SGLT2 inhibitors increase urinary glucose excretion by inhibiting reabsorption of glucose in the kidney.[2] Canagliflozin has proven in short-term studies to lower HbA1c up to 1%, lower blood pressure, and reduce body weight.[2,3] Known adverse events include increased risk for bone fractures, urinary tract infections and genital mycotic infection.[1,2] According to the 2017 American Association of Clinical Endocrinologists and American College of Endocrinology Guideline, SGLT2 inhibitors can be used as initial therapy for glycemic control.[4] In August 2017, long-term data for canagliflozin from the Canagliflozin Cardiovascular Assessment Study (CANVAS) Program revealed additional, previously unknown benefits, but was off-set by additional risk, prompting the FDA to issue a new Black Box Warning.

CANVAS Program

The CANVAS Program combined data from two large, randomized, placebo-controlled trials (CANVAS and CANVAS-R) that compared canagliflozin to placebo. The primary outcome was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.[1] The trials followed 10,142 patients with uncontrolled type 2 diabetes at high risk for cardiovascular disease for a mean of 188.2 weeks. The trials included patients meeting the following criteria: HbA1c between 7% and 10.5%, over 30 years of age with history of prior cardiovascular disease or over 50 years of age with two or more cardiovascular disease risk factors,* and estimated eGFR $\geq$ 30 mL/min/1.73m^2.[6] The baseline characteristics in the canagliflozin and placebo groups were similar. Table 1 summarizes pertinent baseline characteristics.

Patients treated with canagliflozin had a 14% reduced risk of the composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke compared to the placebo group (hazard ratio, 0.86; 95% CI, 0.75 to 0.97; P< 0.001 for noninferiority; P=0.02 for superiority).[5,6] Evaluation of the individual cardiovascular events within the composite outcome did not yield statistically significant results.

Adverse events including volume depletion, diuresis, increased genital mycotic infections and fracture were experienced more often by

patients in the canagliflozin group than placebo, as previously reported.[2] However, a new adverse event was identified during the trial – increased risk of amputation.[6] The risk of amputation almost doubled when patients were treated with canagliflozin, compared to patients treated with placebo (Table 2). The highest absolute risk for amputation occurred among those with a prior amputation or peripheral vascular disease.[6] Amputation of the toe or metatarsal occurred most frequently. The mechanism of canagliflozin in increasing the risk of amputation is undetermined.[6] Due to these results, the FDA issued a Black Box Warning indicating that canagliflozin is associated with increased risk of lower limb amputation.[1]

Summary

Canagliflozin provides numerous benefits including reducing HbA1c, body weight, blood pressure, and risk of cardiovascular events. However, canagliflozin poses a risk for volume depletion, diuresis, increased risk of genital mycotic infection, fractures, and amputation. Before initiating canagliflozin, the FDA advises health care professionals to consider predisposing factors that may put patients at a higher risk of amputation including history of prior amputation, peripheral vascular disease, neuropathy, and diabetic foot ulcers.[1] Patients should be informed of the increased risk of amputations associated with this medication and counseled on the signs and symptoms of infection including new pain or tenderness, sores or ulcers, or infections in lower extremities which could place them at a higher risk for amputations.[1] The risk for amputation was not seen in studies with dapagliflozin and empagliflozin although data are limited.[7]

*Risk factors: duration of at least 10 years of diabetes, systolic blood pressure higher than 140 mm Hg while receiving any antihypertensive agents, current smoker, microalbuminuria or macroalbuminuria, or high-density lipoprotein cholesterol level of less than 1 mmol per Liter.

Table 1: Baseline Characteristics of participants[6]

Characteristics	Canagliflozin (N = 5,795)	Placebo (N = 4,347)
Mean age, years	63.2	63.4
Female, %	35.1	36.7
Race, %		
White	77.8	79.0
Asian	13.4	11.7
Current smoker, %	17.6	18.1
Mean duration of diabetes, years	13.5	13.7
Baseline therapy: Antihyperglycemic agents, %		
Metformin	76.7	77.7
Insulin	49.9	50.7
Sulfonylurea	43.6	42.2
DPP-4 inhibitor	12.0	13.0
GLP-1 receptor agonist	3.8	4.3
HbA1c, %	8.2	8.2
Hypertension, %	89.5	90.6
History of Cardiovascular disease, %	64.8	66.7
Baseline therapy: Cardioprotective agents, %		
RAAS inhibitor	80.2	79.8
Statin	74.7	75.2
Antithrombotic	73.0	74.4
Beta blocker	52.4	54.8
Diuretic	43.8	45.0

Table 2: Amputations experienced by participants[8]

	Canagliflozin, event rate 1000 patient-years	Placebo, event rate 1000 patient-years	Hazard ratio (95% CI)
All amputation	6.30	3.37	1.97 (1.41-2.75)
Minor amputation	4.48	2.44	1.94 (1.31-2.88)
Toe	3.44	2.16	
Transmetatarsal	1.03	0.29	
Major amputation	1.82	0.93	2.03 (1.08-3.82)
Ankle	0.04	0.07	
Below-knee	1.16	0.64	
Above-knee	0.62	0.21	
History of amputation			
Yes	96.30	59.16	2.15 (1.11-4.19)
No	4.68	2.48	1.88 (1.27-2.78)
History of PVD			
Yes	12.09	8.16	1.39 (0.80-2.40)
No	5.20	2.41	2.34 (1.53-3.58)

References

1. U.S. Food and Drug Administration. FDA confirms increased risk of leg and foot amputations with the diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR). U.S. Food and Drug Administration Home Page. https://www.fda.gov/Drugs/DrugSafety/ucm500965.htm. Published May 17, 2017. Accessed September 21, 2017.
2. American Diabetes Association. Standards of Medical Care in Diabetes – 2017. Diabetes Care. 2017;40(Suppl. 1):S1–S2:1-142.
3. Nathan N, Ahmed-Sarwear N, Werner P. SGLT-Inhibitors: A Novel Mechanism in Targeting Glycemic Control in Type 2 Diabetes Mellitus. The Consultant Pharmacist. 2016;31(5):251-260.
4. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm - 2017 Executive Summary. Endocr Pract. 2017;23(2):207-238.
5. Lee S. Update on SGLT2 Inhibitors-New Data Released at the American Diabetes Association. Crit Pathw Cardiol. 2017;16(3):93-95.
6. Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017.
7. Fadini G, Avogaro A, SGLT2 inhibitors and amputations in the US FDA Adverse Event Reporting System. The Lancet. 2017;5(10):680-681.
8. Neal B, Perkovic V, Mahaffey KW, et al. Supplementary Appendix: Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes. N Engl J Med. 2017

HYPOGLYCEMIA IN OLDER ADULTS: CURRENT AND FUTURE DIRECTIONS

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On September 12, 2017, the Food and Drug Administration (FDA) sponsored a symposium concerning the risk of hypoglycemia in older adults (≥ 65 years) with diabetes.[1] The symposium provided attendees with information regarding hypoglycemia and symptom recognition in the elderly, risks of poor clinical outcomes, as well as current and future directions to address the problem of hypoglycemia. Hypoglycemia is characterized as a drop in blood glucose below normal, defined as ≤70 mg/ml.[2] Older adults are at greater risk of hypoglycemia compared to other age groups. [3,4] A recent article published by the Journal of the American Medical Association found that patients greater than 80 years old with insulin-dependent diabetes, were more than twice as likely to visit the emergency department and five times more likely to be hospitalized than individuals aged 45-64 years old. [4] Precipitating factors for emergency department visits related to hypoglycemia include: meals (skipped meals or inadequate carbohydrate content), using the wrong insulin product (such as using short acting insulin instead of long acting), administering the wrong dose or confusing dosing units, accidentally getting an extra insulin dose, and pump misadventures. [4] Older adults with diabetes are also at greater risk for polypharmacy and developing geriatric syndromes secondary to diabetes such as cognitive impairment, urinary incontinence, injurious falls, and continuous pain in comparison to non-diabetic older adults.[1,5]

Hypoglycemic symptoms in the elderly are often nonspecific and can be easily misdiagnosed as stroke, vertigo, or visual disturbances.[5] In the elderly patient with dementia, symptoms can additionally be misinterpreted as dementia-related confusion and agitation.[1,5] Patients with dementia may also be less able to verbally communicate their symptoms to caregivers. Previous trials have shown severe hypoglycemia to be strongly linked with increased risks of many poor clinical outcomes in patients with diabetes, including vascular events and death. [6] In older adults specifically, hypoglycemia can result in traumatic falls, fractures, and cognitive dysfunction.[7] Hypoglycemia has also been linked to ST depression, QTc prolongation, and flattening of the T-wave. [8,9] Therefore, the treatment goal for diabetes management in older adults is to obtain a balance between glycemic control and to prevent/decrease the progression of acute and chronic complications, while avoiding hypoglycemia. [1,7] However, it is crucial to remember that aggressive diabetes management may not be appropriate for older adult patients and may affect patient comfort, safety, and overall quality of life, while not necessarily improving outcomes. Hemoglobin A1C, the primary therapeutic goal in guidelines, does not correlate with hypoglycemia risk in older adults; in fact, hypoglycemia has been shown to be common at all levels of A1C.[1,7,10]

National efforts to address hypoglycemia in the elderly will likely include surveillance, prevention, incentives, oversight, and research. The Centers for Medicare and Medicaid Services have discussed hypoglycemia being a possible future performance measure. [1] The FDA has developed an Adverse Drug Events action plan, which includes antidiabetic medications to avoid in order to prevent hypoglycemia. [11] The Department of Veterans Affairs has rolled out the National Hypoglycemic Safety Initiative.[12] Future research endeavors aim to highlight an expanding role for continuous glucose monitoring (CGM) in providing patients with optimal diabetic care. In research specifically, CGM can help to measure the clinical effects of asymptomatic hypoglycemia and potentially reduce the risk of hypoglycemic and hyperglycemic events.[13] Symposium stakeholders widely

agreed that hypoglycemia should be realized as an outcome measure in and of itself, as opposed to a side effect. The FDA communicated its intent to stay involved in the development of those initiatives to avoid hypoglycemia. [1]

References
1. Reducing the Risk of Preventable Adverse Drug Events Associated with Hypoglycemia in Older Populations. U.S. Food & Drug Administration. FDA Symposium. FDA White Oak Campus, MD. September 12, 2017.
2. American Diabetes Association. Standards of Medicare Care in Diabetes – 2017. Journal of Clinical and Applied Research and Education 2017. Vol 40: S1-S135.
3. Sue Kirkman M, Briscoe VJ, Clark N, et al; Consensus Development Conference on Diabetes and Older Adults. Diabetes in older adults: a consensus report. J Am Geriatr Soc. 2012;60(12):2342-2356.
4. Geller AI, Shehab N, Lovegrove MC, et al. National estimates of insulin-related hypoglycemia and errors leading to emergency department visits and hospitalizations. JAMA Intern Med. 2014;174(5):678-686.
5. Abdelhafiz AH, Rodríguez-Mañas L, Morley JE, Sinclair AJ. Hypoglycemia in Older People - A Less Well Recognized Risk Factor for Frailty. Aging and Disease. 2015;6(2):156-167. doi:10.14336/AD.2014.0330.
6. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008;358:2545-2559
7. Joslin Diabetes Center. Joslin Diabetes Center and Joslin Clinic guideline for the care of the older adult with diabetes. 2015.
8. Beom JW, Kim JM, Chung EJ, et al. Corrected QT Interval Prolongation during Severe Hypoglycemia without Hypokalemia in Patients with Type 2 Diabetes. Diabetes & Metabolism Journal. 2013;37(3):190-195. doi:10.4093/dmj.2013.37.3.190.
9. Lindstrom T, Jorfeldt L, Tegler L, Arnqvist HJ. Hypoglycaemia and cardiac arrhythmias in patients with type 2 diabetes mellitus. Diabet Med. 1992;9:536–541
10. Lipska KJ, Warton EM, Huang ES, et al. HbA1c and risk of severe hypoglycemia in type 2 diabetes: the Diabetes and Aging Study. Diabetes Care. 2013;36(11):3535-3542.
11. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. (2014). National Action Plan for Adverse Drug Event Prevention. Washington, DC:
12. U.S. Department of Veterans Affairs. Hypoglycemia safety initiative (HIS). 2015. Washington DC.
13. Meade LT. The use of continuous glucose monitoring in patients with type 2 diabetes. Diabetes Technol Ther. 14:190–195, 2012

A NEW FLUOROQUINOLONE: DELAFLOXACIN (BAXDELA™)

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In June 2017, delafloxacin (Baxdela™) received FDA approval for treatment of adult patients with acute bacterial skin and skin structure infections (ABSSSI). It was given priority review due to its designation as a Qualified Infectious Disease Product (QIDP). QIDP designation is used by the FDA to encourage the development of new antibiotics.[1] Delafloxacin has activity against most gram-positive organisms (e.g. *Staphylococcus* spp., *Streptococcus* spp., *and Enterococcus faecalis),* some *gram-negative organisms (e.g.Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae,* and to an extent, *Pseudomonas aeruginosa*), anaerobes (e.g. *Bacteroides* spp., *Prevotella* spp., and *Clostridium difficile*), and atypical respiratory tract pathogens (*Legionella, Chlamydia,* and *Mycoplasma)*.[2,3,4] However, unlike other fluoroquinolones,

delafloxacin has additional antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA).[3] A review of delafloxacin's mechanism of action, pharmacokinetics, clinical trials leading to FDA approval, safety, and potential role will be discussed.

Similar to other fluoroquinolones, delafloxacin exhibits bactericidal activity by inhibiting bacterial topoisomerase IV and DNA gyrase (topoisomerase II), therefore blocking replication.[4,5] Delafloxacin has no active metabolites and is predominately unchanged in the plasma. The intravenous (IV) formulation is eliminated primarily by renal excretion with 65% unchanged in the urine and 28% unchanged in the feces, whereas the oral formulation is excreted 50% unchanged in the urine and 48% unchanged in the feces.[5] Its clearance is reduced in patients with moderate and severe renal impairment, therefore dosage adjustment should be considered for patients taking the IV formulation with estimated glomerular filtration rate (eGFR) of 15 to 29 mL/min/1.73 m^2. There is no dosage adjustment for renal impairment with delafloxacin tablets. No adjustment is necessary for hepatic impairment with either formulation. Delafloxacin is available in 450 mg tablets and 300 mg powder for injection that requires reconstitution and dilution. The bioavailability of a single 450 mg tablet is comparable to that of a single 300 mg intravenous dose.[4] The recommended dose for treatment of ABSSSI is 300 mg IV infusion over 1 hour every 12 hours or 450 mg oral tablet every 12 hours for 5 to 14 days.[4] Dosing of 200 mg IV every 12 hours is recommended for patients with eGFR 15 to 29 mL/min/1.73 m^2 and is not recommended for use in patients with eGFR < 15 mL/min/1.73 m^2. Like other fluoroquinolones, the administration of delafloxacin should be separated from sucralfate, antacids or multivitamins containing magnesium, aluminum, zinc, iron, or with didanosine buffered tablets by at least two hours before or six hours after.[4,5]

In two phase III, randomized, double-blind, multinational, multicenter, non-inferiority, active comparator clinical trials, the safety and efficacy of delafloxacin was compared with vancomycin plus aztreonam for the treatment of ABSSSI. A total of 1510 patients were treated for 5 to 14 days with either delafloxacin or vancomycin 15 mg/kg of body weight plus aztreonam.[3,4] In the first study, IV delafloxacin 300 mg twice daily was compared with vancomycin plus aztreonam. The second study was similar to the first, however, patients receiving delafloxacin 300 mg IV every 12 hours for 6 doses were then switched to delafloxacin 450 mg tablets every 12 hours. The primary outcome of both trials was clinical response at 48-72 hours defined by a ≥ 20% decrease in lesion size spread in the area of erythema, as determined by digital planimetry. Both studies included a distribution of patients with hypertension, diabetes, renal impairment, and/or current or recent history of drug abuse.[4] Patients in both trials had the following infections: cellulitis, wound infection, major cutaneous abscess, and burn infection. The overall mean surface area of the infected lesion was 307 cm^2 and 353 cm^2 for trial 1 and trial 2, respectively. Delafloxacin was found to be non-inferior to vancomycin plus aztreonam in both trials with clinical response rates of 78.2% versus 80.9% in the first trial, and 83.7% versus 80.6% in the second trial.[4,5] In study 1 and study 2 mean difference between delafloxacin and vancomycin plus aztreonam was -2.6%, 95% CI [-8.8, 3.6] and 3.1%, 95% CI [-2.0, 8.3], respectively.[5]

The most common adverse events reported from the aforementioned phase III trials were nausea (8%), diarrhea (8%), headache (3%), transaminase elevations (3%), and vomiting (2%).[5] A standard fluoroquinolone FDA boxed warning is included on the label: tendinitis and tendon rupture, peripheral neuropathy, CNS effects, and exacerbation of myasthenia gravis.[5] It should be noted that unlike other fluoroquinolones in its class, QT prolongation nor photosensitivity was observed when tested.[3]

The spectrum of activity of delafloxacin is most similar to levofloxacin, with the addition of having MRSA coverage. Although the broad

antimicrobial spectrum of delafloxacin may prove very useful for polymicrobial infections in the outpatient setting, its place in therapy is yet to be determined. Caution should be considered in regards to its general empiric use, unnecessarily adding to fluoroquinolone resistance and increasing the risk for *Clostridium difficile* infection associated with this class.[5] Therefore, delafloxacin should not be considered for first line treatment of ABSSSI and may be considered for use in more serious infections, in which study results are still pending.

References
1. United States Government Accountability Office. Antibiotics: FDA Has Encouraged Development, but Needs to Clarify the Role of Draft Guidance and Develop Qualified Infectious Disease Product Guidance. http://www.gao.gov/assets/690/682391.pdf (accessed 2017 Nov 6).
2. Van Bambeke F. Delafloxacin, a non-zwitterionic fluoroquinolone in phase III of clinical development: evaluation of its pharmacology, pharmacokinetics, pharmacodynamics and clinical efficacy. *Future Microbiol.* 2015;10: 1111-23.
3. McCurdy S, Lawrence L, Quintas M, et al. *In vitro* activity of delafloxacin and microbiological response against fluoroquinolone-susceptible and nonsusceptible *Staphylococcus aureus* isolates from two phase 3 studies of acute bacterial skin and skin structure infections. *Antimicrob Agents Chemother*. 2017;61:e00772-17.
4. Delafloxacin prescribing Information (Baxdela). Melinta Therapeutic Inc. Lincolnshire, IL. 2017.
5. FDA. Baxdela (delafloxacin) Tablets and Injection – Medical Reviews. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208610Orig1s000,208611Orig1s000SumR.pdf (accessed 2017 Aug 29).

DC-CCP FALL RESIDENCY SERIES EVENT RE-CAP

Jessica Szatkowski, 2nd year Student Pharmacist, Shenandoah University Bernard J. Dunn School of Pharmacy, DC-CCP Residency Series Co-Chair

On Thursday, November 2nd, the DC-CCP Residency Series Committee held their first event of the year, a Residency Roundtable. The event was held at Shenandoah University's Winchester campus and simultaneously broadcast via Facebook Live to Shenandoah's Fairfax campus, the University of Maryland, and Howard University. Over thirty pharmacy students across the DMV were able to participate in the discussion using the unique connectivity of the Facebook Live platform. The Residents who presented were Dr. Nichelle Logan, a PGY-1 Community Pharmacy Resident at Valley Pharmacy and Dr. David Logan and Dr. Molly Rincavage, both PGY-1 Pharmacy Practice Residents at Valley Health in Winchester, VA. The archived live stream event can be found at the following link: http://bit.ly/2jSHAkK

The committee will be hosting two more events during this 2017-2018 academic year: a fellowship seminar tentatively scheduled for the end of January, and a Residency Director Round Table in March. Each event will be live broadcast to member schools. The Residency Series Committee encourages pharmacy students to explore post-graduate opportunities and to use the resources available to them through DC-CCP and ACCP.

Special thanks to our peer reviewers:

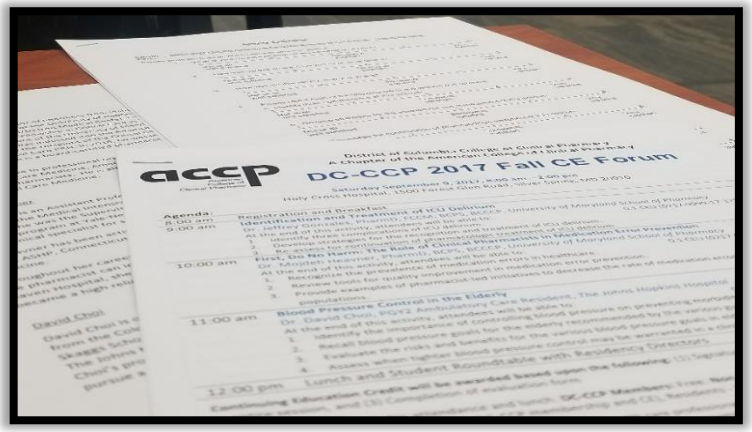
Christine Darby, PharmD, BCACP
Gloria Kang, PharmD, MBA, BCPS
Jessica Merrey, PharmD, MBA, BCPS, BCACP, BCGP
Jessica Pyhtila, PharmD, BCPS, BCGP

Interested in contributing an article for the DC-CCP Winter newsletter or becoming a peer reviewer?

Please contact **dcccpnewsletter@gmail.com**

Upcoming Events

Thank you to all who attended our National's Game Networking Event and Fall CE Forum! Stay tuned for additional CE and networking events including a brewery tour in January 2018!



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