Volume 2 | Issue 1
October 2016

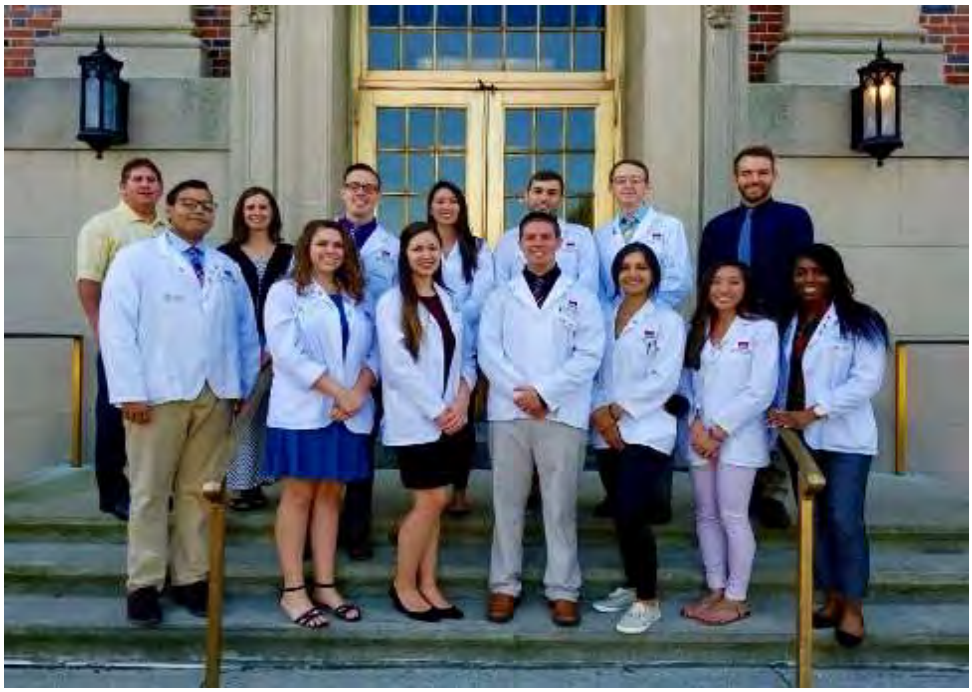
NYS-ACCP Insider

Albany College of Pharmacy and Health Sciences

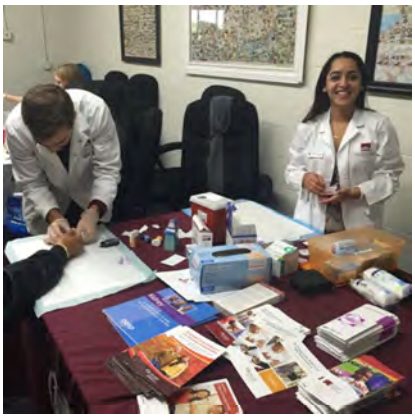
Special points of Interest:

- Synopsis of the ACPHS-ACCP Student Chapter
- NYS-ACCP Research Grant
- CDC Opioid Guideline Review
- Clinical Spotlight: Maggie Montgomery, PharmD
- NeKF: Contributions to Healthcare Award
- The EMPA-REG OUTCOME Study
- 2016 ACC/AHA/HFSA Heart Failure Update

ACPHS-ACCP Student Chapter Synopsis



The student chapter of ACCP at Albany College of Pharmacy and Health Sciences has a central goal of engaging in direct-patient care events for students who are seeking post-graduate training, independent research careers, and academic faculty positions. This patient care goal is fulfilled by our three community outreach programs. Our Cardiovascular and REnal Disease (CaRE) Screenings program, in affiliation with the Northeast Kidney Foundation, allows us to provide free blood pressure measurements, blood glucose, cholesterol, and urinalysis testing, and medication review and counseling to the public across the Capital Region of New York. In order to fully prepare the students for the skills utilized at these screening events, we have developed and offer "CaRE Screening Certification trainings." This training allows the students to learn how to and practice taking a manual blood pressure and a blood glucose measurement. In addition, the students are taught what the values mean and how to educate the community on these values and how they can develop a healthier lifestyle.



Another community outreach program we have developed is "Script Your Future." Events for this program are centered on the importance of medication adherence and preventative health. We address common concerns about why patients may not be adherent to their medications, provide tips on how to remember to take their medications, and inform patients of the possible problems that could occur if they are not adherent. This is accomplished by providing medication adherence tools, including pill organizers, downloadable apps, and blank wallet-sized medication lists. Informational handouts are also provided regarding appropriate vaccine schedules and when to receive a comprehensive screening based on specific age groups to help the community take better control of their health.

Our chapter has recently developed a new community outreach project over the last year known as "Care for KIDneys." These events target elementary and middle school children to educate them on the importance of the kidney and how taking care of their bodies will help prevent future chronic diseases- specifically hypertension, diabetes, and chronic kidney diseases. We provide education through various approaches, including interactive games, word searches and word scrambles. Examples of the games include, true/false and guessing how much sugar are in common drinks. By rewarding them with prizes and utilizing an interactive learning style, the kids are highly responsive to these events. In addition, by teaching kids yoga, this outreach project stresses the importance of exercising and staying health.

In addition to those direct care projects, in order to encourage continued education of our students, we offer Clinical Pharmacy Challenge (CPC) nights throughout the school year. This is our way to help students, specifically those in their professional years, to come and review course material in a fun, interactive way. CPC nights occur three times per semester and includes topics of Self-Care, Infectious Diseases, Endocrine, Nephrology, Cardiology, and Neurology/Psychiatry pharmacotherapies. Students develop questions in a similar format to the Annual ACCP Clinical Pharmacy Challenge. Questions are derived from class material, textbooks, and current practice guidelines, all of which are reviewed by faculty members of the specialty area. The beginning of the night starts with a lightening round, followed by a case vignette, and ends with a jeopardy-style round. Prizes of gift cards or clinical resources are awarded to the 1st and 2nd place teams and at the end of the semester, the top-scoring team is awarded a grand prize.

Overall, our student chapter is highly successful. The community is always appreciative for the services that we provide and the students' involvement is overwhelming.

- **Joe Hamedl, PharmD Candidate, ACPHS Class of 2018**

2016 NYS-ACCP Research Grant Awardee

Congratulations to William Eggleston from SUNY Upstate Medical University for his selection as the winner of the inaugural NYS ACCP research grant. Dr. Eggleston will receive $3000 for his project "Determining the effects of loperamide and n-desmethyl loperamide on cardiac potassium currents and the impact of naloxone on these effects." He will be presenting his findings at the 2017 NYS ACCP Annual Fall Meeting.

Thank you to research grant committee members Norberto Alberto, Ed Bednarczyk, Nicole Acquisto, Curt Haas, Jack Brown, Chris Evans, Lisa Avery, and Leslie Riddle for volunteering to create the proposal criteria and reviewing applications. Please watch your email next spring for the 2017 application details.

- **Katherine Juba, PharmD, NYS ACCP Past President**
  Research Grant Committee Chair

CDC Opioid Guideline Review

CDC Guidelines for Prescribing Opioids for Chronic Pain

The use of opioids for chronic pain has caused major concern for the healthcare world, as this has contributed to addiction, overdoses, and unfortunately many deaths. More than 40 Americans die every day due to prescription opioid overdoses.[1] Approximately 20% of patients experiencing non-cancer related pain are given opioid prescriptions, resulting in the sales of prescription opioids as well as deaths from opioid overdoses to have quadrupled since 1999.[2,3] The CDC released updated opioid guidelines on March 15, 2016, that were published for a primary care audience, since PCPs are the most common prescribers of opioids. Nevertheless with team-based care being of upmost importance for ideal patient care it is important for other health care professionals, including pharmacists, to understand these guidelines. The guidelines are for assessing when and how to prescribe opioid medications for chronic pain, excluding pain due to active cancer, palliative care, or end of life care.[2] Chronic pain is defined as pain that lasts longer than 3 months, or that lasts past the time of normal tissue healing.[4]

Areas of Consideration

There are 12 main recommendations grouped into three different categories to consider when prescribing opioids. These considerations are based upon three principles of improving patient care. This includes non-opioid therapy being the preferred treatment for chronic pain, using the lowest effect dose when opioids are prescribed, and exercising caution when prescribing opioids as well as closely monitoring patients.[1]

Area 1: Determining When to Initiate or Continue Opioids for Chronic Pain

As a first line treatment option, non-opioid therapy and non-pharmacologic therapy is preferred.[4] Opioids should only be prescribed when a prescriber believes that the benefits for pain alleviation and better function will outweigh possible risks.[4] Clearly defined treatment goals/expectations should be outlined before beginning opioid use, and opioids should only be used continually if there are beneficial outcomes that outweigh the risk.[4] These benefits and risks should be discussed with patients throughout therapy so that those involved know their responsibilities.[4] This is an area in which pharmacists can be of great importance, by counseling patients when they receive an opioid prescription on the proper usage as well as probable risks.

Area 2: Opioid Selection, Dosage, Duration, Follow-Up, and Discontinuation

The lowest effective dose of immediate release opioids should be prescribed for chronic pain, rather than extended release/long acting.[4] The dosage should also be closely monitored throughout treatment to determine if adjustments should be made. While these guidelines focus on chronic pain, it is also known that this may often arise from acute pain. When opioids are initiated for acute pain, approximately a 3-7 day supply should be prescribed depending upon the expected duration of initial pain.[4] Once again, continual monitoring of patients on opioid therapy is key. Patients should be evaluated one to four weeks from initial treatment, as well as every few months, to determine if the dosing is correct, as well as if they are experiencing benefits.[4] Pharmacists are also in a position where they can reach out to prescribers if they have any concerns about the use of opioids in a patient. Team-based care is essential to optimize patient care and safety.

Area 3: Assessing Risk and Addressing Harms of Opioid Use

Risk management is vital to improve patient outcomes and decrease adverse events that may occur if opioids are being used improperly, or if the dosing is of possible harm to a patient. If a patient is at greater risk for overdose, either from being on high doses or having a history of overdoses/ substance abuse, the prescriber should consider offering naloxone.[4] The prescriber also has a responsibility to monitor patients through NYS prescription drug monitoring program (PDMP) to help determine if a patient is at risk for overdose.[4] Pharmacists can also assist by tracking opioid prescriptions picked up by patients at their pharmacy to determine if there is concern for a patient. Drug urine tests to test for other drugs that may be of harm should be implemented by physicians.[4] Prescribers are recommended to avoid patients using both opioids and benzodiazepines, and are in a position to assist patients with opioid-use disorder by assessing the need for buprenorphine or methadone.[4]

In Summary: These guidelines were created to get opioid prescribing and use under control with the main focus of improving patient safety. Team-based care is essential for health-care professionals in order to educate, assess, and advise patients on opioid therapy.

References:

1. American Pharmacists Association. CDC issues guidelines to limit opioid analgesic prescriptions. [Internet] March 16, 2016 [cited September 15, 2016]. Available from: https://www.pharmacist.com/cdc-issues-guidelines-limit-opioid-analgesic-prescriptions

2. Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain. [Internet] March 16, 2016 [cited September 15, 2016]. Available from: http://www.cdc.gov/drugoverdose/prescribing/guideline.html

3. Centers for Disease Control and Prevention. Injury Prevention & Control: Opioid Overdose. [Internet] June 21, 2016 [cited September 15, 2016] Available from: http://www.cdc.gov/drugoverdose/data/overdose.html

4. Centers for Disease Control and Prevention. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016: Recommendations and Reports. [Internet] March 18, 2016 [cited September 15, 2016]. Available from https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm

- **Maggie Sullivan, PharmD Candidate, ACPHS Class of 2019**

Clinical Spotlight: Maggie Montgomery, PharmD

Clinical Pharmacist at St. Luke's Cornwall Hospital

What made you interested in clinical pharmacy?
My interest started when I was still in pharmacy school and I shadowed some hospital pharmacists. I liked working in hospital pharmacy because you get so much more information about the patients and have a more complete picture about what is going and their condition. Also, after gaining more knowledge and experience through classes and rotations, I just felt like clinical pharmacy allowed me to better apply everything I've learned. I also like getting to work in a multi-disciplinary team to see different perspectives and contributing to helping the patient.

Did you have a mentor whom you looked up to and how did he/she influence you?
The school I went to, Belmont University College of Pharmacy in Nashville, had a very small class size of 75 so I was really able to get to know the professors and faculty, which I really liked. Throughout school, there wasn't just one person who I saw as a mentor since we were all almost like family and I felt like I could go to any of them depending on the topic.
During my residency, one my preceptors, Dr. Elizabeth Chung, was a great role model to me. She had years of experience and her hard work and dedication was really inspiring. She always had a passion for doing beyond what was expected and challenged everyone to be and do better. I learned so much from the way she practiced.

"As clinical pharmacists, we need to be eager to learn and be able to adapt so we can do better for our patients."

What extracurricular activities were you involved with in pharmacy school?
I was very active and was mainly involved in the American College of Clinical Pharmacy (ACCP), American Society of Health-System Pharmacists (ASHP), American Pharmacists Association (APhA), Phi Lambda Sigma (PLS), Kappa Psi and Rho Chi. I had a variety of different leadership roles in each organization. I was the secretary for PLS, the service/fundraising chair of ASHP, and the social chair of my pharmacy class.

What is your current practice/role?
I've just finished my residency at the Veterans Affairs New York Harbor Healthcare Systems in New York and plan on getting my BCPS certification soon. I've only been in my position at St. Luke's for two months, so everything is still new. I am also the only clinical pharmacist at the hospital so people come to me with various different projects. My biggest role right now is in the ICU, doing rounds and being a part of a team to manage the patients. One major program that the hospital is working on implementing is antimicrobial stewardship. This is going to become a larger part of my role in the hospital as I work with one of the infectious disease physicians to get this program off the ground. We're also doing a Drug Utilization Evaluation on fluoroquinolones to see how appropriate our use is right now, especially with the release of the new FDA warning. However, this is just the beginning and I still have much room for growth and development.

How do you keep up with the latest findings and advancements in clinical pharmacy?
I am fortunate enough to work in an environment where everyone holds each other to such a high standard so we all stay informed on various subjects, and then in turn we keep each other updated. My favorite journal to stay current is the *P&T Journal* and I also subscribe to the ACCP Pharmacotherapy Newsletter to keep myself updated. I also utilize the Greater New York hospital Association (GNYHA) e-mail alerts and CE's. I'm still relatively new at this so I'm still figuring out the best way to keep up since there's so much information out there!

What advice would you give to a student pursuing a career in clinical pharmacy?
I would say to just be curious and keep an open mind. In school, we learn so much and are overwhelmed with so much knowledge but there's still so much information out there! As clinical pharmacists, we need to be eager to learn and be able to adapt so we can do better for our patients. There's always something new to be learned as medicine gets more advanced. It is important to maintain interest in our field and remember why we got into this profession – to help people. As medical professionals it is our responsibility to know the best way to help our patients.

- **Nelson Polanco and Anne Lau, PharmD Candidates, ACPHS Class of 2018**

Northeast Kidney Foundation: Contributions to Healthcare

The Northeast Kidney Foundation (NeKF) recently awarded Albany College of Pharmacy and Health Sciences (ACPHS) the Contributions to Healthcare Award. The College has had a relationship with the NeKF since 2011 and with the help of executive director Carol LaFleur as well as faculty members at ACPHS, has been able to coordinate numerous services to the renal community over the years. With ACPHS faculty serving on the NeFK's Board of Trustees, as well as on the Medical Advisory Committee, faculty and students are able to provide clinical and consultative services to the NeKF community screening and educational programs. Both faculty and students have been active participants in the NeKF's annual advocacy day for the past ten years. The focus of the services is to help those affected by kidney disease, the conditions associated with it and to provide education and knowledge for the community. Some of the services that the college has provided with the NEKF include CaRE Screenings, which aimed to assess those at risk for kidney-related problems by performing blood pressure readings, as well as blood glucose testing. Student pharmacists, under the guidance of a faculty member, help to provide information and resources on how to minimize one's risk for disease or reduce progression of kidney disease, in addition to promoting healthy lifestyles. At another volunteer event, the Kidney Foundation 5K, volunteers helped register participants as well as collect vitals. Because of the college's consistent dedication in partnering with the NeKF, ACPHS was honored to receive the Contributions to Health Care Award, which was accepted by College President, Dr. Greg Dewey.

- **Kenneth Ng, PharmD Candidate, Class of 2018**

Have a Heart, Save a Kidney – The EMPA-REG OUTCOME Study

The endocrinology, cardiology, and nephrology world can hardly contain their excitement with the recent updates in regards to empagliflozin (Jardiance) use in patients with type 2 diabetes (T2DM) at high risk for cardiovascular (CV) events. CV disease and renal disease have a common denominator in that diabetes is a major risk factor. Furthermore, CV disease is the leading cause of death in the United States.[1] Finding a treatment regimen that could reduce the complications of diabetes, especially macrovascular complications, is considered the holy grail of diabetes management.

What is empagliflozin?

Empagliflozin is a sodium-glucose co-transporter 2 (SGLT2) inhibitor which exhibits its effects in the kidneys, lowering the renal threshold for glucose excretion.[2,3] It is indicated as adjunct therapy to diet and exercise to improve glycemic control in adults with T2DM.[2,3]

Already known benefits of empagliflozin therapy include decreasing glycated hemoglobin (A1c) by 0.7% – 1.1%, reducing fasting and postprandial glucose, inducing weight loss, and lowering blood pressure.[2,4,5,6] Common adverse reactions include, but are not limited to, urinary tract infections, female genital mycotic infections, and hypotension associated with the glycosuric effect of the medication.[2,3] Furthermore, it is not recommended to initiate empagliflozin if the estimated glomerular filtration rate (eGFR) is < 45 mL/min/1.73m^2 and should be discontinued (for those already on empagliflozin) if eGFR persistently falls below 45 mL/min/1.73m^2.[2,3]

What does the EMPA-REG OUTCOME trial tell us?

The EMPA-REG OUTCOME trial was a multicenter, randomized, double-blind, placebo-controlled study. The study explored the effect of empagliflozin 10 mg or 25 mg once daily versus placebo on CV events in adults with T2DM at high risk for CV events who were receiving standard care.[6,7] Standard care was defined as treating CV risk factors such as dyslipidemia and hypertension according to local guidelines.[6,7] To note, 73.8% of patients who received empagliflozin were taking metformin at baseline and throughout the study.[8]

Major inclusion criteria were body mass index ≤ 45 kg/m^2, eGFR ≥ 30 mL/min/1.73m^2, patients with an A1c of 7% – 9% not receiving glucose lowering agents and patients with an A1c of 7% – 10% receiving stable glucose lowering agents for at least 12 weeks prior to randomization.[6,7,8] To note, this is not an all-inclusive list of the inclusion criteria.[8]

The primary outcome was a composite of death from CV causes, non-fatal myocardial infarction (MI) (excluding silent MI), or non-fatal stroke.[6,7] The key secondary outcome was a composite of primary outcomes plus hospitalization for unstable angina.[6,7] Other secondary outcomes included a composite of renal microvascular outcomes (June 2016 update).[7]

A total of 7020 patients were treated and included in the primary analysis with a median observation time of 3.1 years. The trial was designed as a non-inferiority study for the primary outcome. However, if the non-inferiority endpoint was met for the primary and key

secondary outcome, the authors could proceed to assess the superiority of empagliflozin compared to placebo for the primary outcome. The trial continued until an adjudicated primary outcome occurred in at least 691 patients powering the study at 90%.[6,7]

The CV and mortality results from the original EMPA-REG study published September 2015 were so compelling, it prompted a June 2016 publication further evaluating the effects of empagliflozin on the progression of kidney disease. The main results from both updates can be found in the Risk Comparison for 2015 and 2016 EMPA-REG Updates table below.

Risk Comparison for 2015 and 2016 EMPA-REG Updates

September 2015 EMPA-REG OUTCOME Update [5,8]				*June 2016 EMPA-REG OUTCOME Update* [6,7,9]			
Outcome	**RRR**	**ARR**	**P-value**	**Outcome**	**RRR**	**ARR**	**P-value**
Primary Composite Outcome	14%	1.6%	<0.001 (non-inferiority); 0.04 (superiority)	**Secondary Composite Renal Microvascular Outcome**	38%	14%	<0.001
Key Secondary Outcome	11%	1.5%	<0.001 (non-inferiority); 0.08 (superiority)	**Incident or Worsening Nephropathy**	39%	6.1%	<0.001
Death from CV Causes	38%	2.2%	<0.001	**Progression to Microalbuminuria**	38%	5%	<0.001
Death from Any Cause	32%	2.6%	<0.001	**Initiation of Renal Replacement Therapy**	55%	0.3%	0.04
Hospitalizations for Heart Failure	35%	1.4%	0.002	**Doubling of Serum Creatinine Accompanied by eGFR ≤ 45 mL/min/1.73m²**	44%	1.1%	<0.001

Abbreviations: eGFR – estimated glomerular filtration rate; RRR – relative risk reduction; ARR – absolute risk reduction

P-value of 0.05 indicated statistical significance.[6] Renal function over time was analyzed using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[7]

No statistical significance was found in the rates of MI, stroke, incidence of albuminuria, or key secondary outcomes.[6,7] The incidence of non-fatal stroke was greater in the empagliflozin group, although not statistically significant (P-value = 0.16). As expected, there was an increased rate of genital infections in the empagliflozin group (placebo group 1.8%, empagliflozin group 6.4%, P-value <0.001), but no increase in other adverse events.[6] A subgroup analysis for the primary outcome and CV death revealed that out of 3459 (73.8%) patients taking metformin during the trial, 344 patients experienced the primary outcome (hazard ratio 0.92, RRR 8%, P-value 0.14).[8]

The number needed to treat to prevent one primary outcome and one death from any cause over three years was 69 and 39 patients, respectively![6,7,10]

Are the results from EMPA-REG clinically significant?
Definitely! The results from the EMPA-REG trial are compelling enough to provoke a change in the way providers approach pharmacotherapy management in adult patients with T2DM at high CV risk. Overall, there was a reduction in the composite primary outcome (death from CV causes, nonfatal MI, and nonfatal stroke) and the secondary outcome (slowing in the progression of renal disease) when empagliflozin was added to guideline-recommended medical therapy for CV risk reduction.

Metformin is generally considered first line in adults with T2DM unless the patient has a contraindication.[4,11] The use of additional or alternative agents is at the discretion of the provider and based on patient co-morbidities and contraindications.[4,11] Both publications may have some providers considering empagliflozin to be the second line adjunctive option to metformin therapy.

There are some limitations to the study such as not being able to generalize the findings to all populations (cannot generalize to the black population) or patients with T2DM at low risk for CV events. In addition, this is only one study that demonstrated a reduction in cardiovascular death, nonfatal MI, and nonfatal stroke. The strengths empagliflozin demonstrated through this study outweigh the limitations and are illustrated by the statistically significant relative risk reductions found in each update.

Look for more CV outcomes trials with SGLT2 inhibitors to come (canagliflozin and the CANVAS trial; dapagliflozin and the DECLARE-TIMI 58 trial).

References:

1. Centers for Disease Control and Prevention (CDC). National center for health statistics – leading causes of death [Internet]. 2016 [cited 2016 Sep 27]. Available from: www.cdc.gov/nchs/fastats/leading-causes-of-death.htm.
2. Empagliflozin: [package insert]. Ridgefield {CT}: Boehringer Ingelheim Pharmaceuticals Inc; 2016.
3. Empagliflozin. In: Lexi-drugs online [database on the Internet]. Hudson (OH): Lexicomp, Inc.; 2016 [updated 10 Aug 2016]. Available from: http://online.lexi.com. Subscription required to view.
4. American Diabetes Association. Standards of Medical Care in Diabetes 2016. ADA. 2016 Jan; 39(Suppl 1):S1-112.
5. Baker WL, Smyth LR, Riche DM, et al. Effects of sodium-glucose co-transporter 2 inhibitors on blood pressure: a systematic review and meta-analysis. J Am Soc Hypertens. 2014;8(4):262-75.
6. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117-28.
7. Wanner C, Inzucchi SE, Lachin JM, et al. Empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med 2016;375:323-34.
8. Zinman B, Wanner C, Lachin JM, et al. Supplement to empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 2015;373:2117-28.
9. Wanner C, Inzucchi SE, Lachin JM, et al. Supplement to empagliflozin and progression of kidney disease in type 2 diabetes. N Engl J Med. 2016;375:323-34.
10. Karla S. One small step for emplagliflozin, one giant leap for diabetology. Diabetes Ther 2015;6(4):405-409.
11. Garber AJ, Abrahamson MJ, Barzilay JI, et al. Consensus statement by the American association of clinical endocrinologist and American college of endocrinology on the comprehensive type 2 diabetes management algorithm – 2016 executive summary. Endocr Pract. 2016;22(1):84-113.

- **Odirichukwu Duru, PharmD Candidate: ACPHS Class of 2018**

2016 ACC/AHA/HFSA Update on New Pharmacological Therapy for Heart Failure

In April of this year, the American College of Cardiology (ACC), American Heart Association (AHA), and the Heart Failure Society of America (HFSA) published an updated guideline for the management of heart failure[1]. They recognized that the introduction of an angiotensin receptor-neprilysin inhibitor (ARNI) (sacubitril/valsartan (Entresto) and a sinoatrial node modulator (ivabradine (Corlanor)), complement established pharmacologic and device-based therapies for patients with heart failure with a reduced ejection fraction (HF*r*EF).

ARNI

For patients with chronic HF*r*EF, the update provides a **class I recommendation** emphasizing the strategy of inhibiting the renin-angiotensin system with either an ACEI (*LOE A*), an ARB (*LOE A*) or an ARNI *(LOE B-R)* in conjunction with evidence-based beta blockers, and aldosterone antagonists in the appropriate patients, to reduce morbidity and mortality.

The addition of ARNIs is based on data from the PARADIGM-HF trial, which is a randomized controlled trial (RCT) that compared sacubitril/valsartan with enalapril in symptomatic patients with HF*r*EF tolerating an adequate dose of either an ACE inhibitor or ARB. The ARNI reduced the composite endpoint of cardiovascular death or HF hospitalization by 20% (p-value<0.05). The benefit was seen for both death and HF hospitalization and was consistent across subgroups[2]. Therefore, the results of this trial resulted in a **class I recommendation (*LOE B-R*)** to replace an ACE inhibitor or ARB with an ARNI in patients with chronic symptomatic HF*r*EF, NYHA class II or III, to further reduce morbidity and mortality. Although there is strong data favoring the use of ARNIs, these medications do have risks. Concomitant use of ARNIs with ACE inhibitors or within 36 hours of the last ACE inhibitor dose should be avoided. ARNI use is also contraindicated in patients with a history of ACEi induced angioedema and in those with ARB induced angioedema. ARNIs are associated with an increased risk of hypotension, hyperkalemia, and renal insufficiency as well[2]. To note, the updated level of evidence, "*B-R"* indicates that there is "moderate-quality evidence from 1 or more RCTs[1]."

IVABRADINE

The guideline update provides a **class IIa recommendation** for the use of ivabradine (Corlanor) (*LOE B-R)* to reduce HF hospitalization for patients with symptomatic (NYHA class II-III) stable chronic HF*r*EF (LVEF ≤35%) who are receiving guideline-directed evaluation and management (GDEM), including a beta blocker at maximum tolerated dose, and who are in sinus rhythm with a resting heart rate of 70 bpm or greater. Ivabradine is a new therapeutic agent that selectively inhibits the I_f current in the sinoatrial (SA) node, thereby reducing heart rate. The SHIFT trial, a RCT, demonstrated that the benefit of ivabradine was driven mainly by the reduction in HF hospitalization[3]. It included patients with HF*r*EF (NYHA class II-IV, although only a very modest representation of NYHA class IV HF) and left ventricular ejection fraction (LVEF) ≤35%, in sinus rhythm with a resting heart rate of ≥70 bpm. Those with a myocardial infarction within the preceding 2 months were excluded from the trial. It is important to note that due to the well-proven mortality benefits of beta blocker therapy, these agents should be initiated and titrated up to target doses, as tolerated, before assessing resting heart rate for consideration of ivabradine use.

Ivabradine is unique in that it is titrated to heart rate. The goal range is between 50-60 bpm. Since this medication can reduce heart rate, it is contraindicated in patients with acute HF, AV block, bradycardia, hypotension, and sick sinus syndrome. Common adverse effects are atrial fibrillation (8.3%)[5], and bradyarrhythmias, therefore, it is recommended to monitor the patients' cardiac rhythm. It is important to monitor the patients' heart rate especially if using other negative chronotropic agents such as beta blockers or non-DHP calcium channel blockers.

References:
1. Yancy CW, Jessup M, Bozkurt B, et al. 2016 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol.* 2016. doi:10.1016/j.jacc.2016.05.011.
2. McMurray JJV, Packer M, Desai AS, et al. Angiotensin-Neprilysin Inhibition versus Enalapril in Heart Failure. N Engl J Med 2014; 371:993-1004
3. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomized placebo-controlled study. Lancet. 2010 Sep 11;376(9744):875-85.
4. Entresto (sacubitril/valsartan) package insert. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; 2015 Aug.
5. Corlanor (Ivabradine) package insert. Thousand Oaks, CA: Amgen Inc.; 2015 Apr.

- **MaCullen Cope, PharmD Candidate, ACPHS Class of 2018**

Questions? Please contact:
Amanda Winans, PharmD
NYS-ACCP Treasurer
Amanda.Winans@bassett.org

A special thanks to:
Albany College of Pharmacy and Health Sciences – Student ACCP Chapter E-Board
Dr. Kate Cabral, Dr. Michael Kane and Dr. Matthew Stryker, editors
Victoria Ostrovskiy, PharmD Candidate, ACPHS Class of 2018, layout, design and graphics