EMPA-REG Outcome Recap

By: Sapna Shah, PharmD

Diabetes currently affects more than 29.1 million people worldwide. This silent killer disease slowly leaves an imprint in cells affecting vasculature and target organs predisposing patients to the future development of microvascular and macrovascular complications. With this mind, cardiovascular (CV) outcomes trials in diabetes management have become largely favorable.

The EMPA-REG OUTCOME trial results were released at a conference this September; the applause and excitement following indicated that this data was truly remarkable and some even considered it a landmark trial.

7020 patients were randomized to receive empagliflozin 10 mg, empagliflozin 25 mg, or placebo once daily for a median follow-up of 3.1 years. Patients that were included had T2DM and high CV risk – almost half had prior history of myocardial infarction. They were at least 18 years old, primarily Caucasian males (~71%) with glycosolyated hemoglobin (A1C) levels of 8.07%. Approximately 95% of patients were also on antihypertensive medications. 97% of patients completed the study.

The primary outcome of three point major adverse cardiac events (3P-MACE) occurred in 10.5% (490/4687) of patients in the pooled empagliflozin group vs 12.1% (282/2333) in the placebo group. The pooled empagliflozin group had a hazard ratio (HR) of 0.86 (95% CI, 0.74 to 0.99) and *p*=0.04 for superiority. The secondary outcome of four point (4P-) MACE occurred in 12.8% (599/4687) in the empagliflozin group vs 14.3% (333/2333) in the placebo group (HR of 0.89 (95% CI, 0.78 to 1.01 and *p*= 0.04 for superiority). Compared to placebo, empagliflozin did provide small reductions in weight and blood pressure and a greater A1C reduction.

The greatest risk reduction was observed with the secondary outcome of CV death; there was a 38% reduction with empagliflozin (3.7% vs 5.9% placebo). A 32% reduction was observed with all-cause mortality for empagliflozin (5.7% vs 8.3% placebo), and a 35% risk reduction in hospitalization for heart failure with empagliflozin (2.7% vs 4.1% placebo). There were however, no differences in the rate of MI and stroke, creating more mystery around the probable mechanisms of risk reduction in CV death.

Patients had similar rates of adverse events, serious adverse events and discontinuation across both groups. Genital infections, as expected, were reported more frequently in the empagliflozin group (6.4% vs 1.8% placebo). Confirmed hypoglycemia (27.8% empagliflozin vs 27.9% placebo), DKA (0.1% vs <0.1%), and bone fractures (3.8% vs 3.9%), were similar across both groups. Acute renal failure, however, was lower in the pooled empagliflozin group (5.2% vs 6.6%), and renal function was also maintained with empagliflozin

These results have been enticing for clinicians and researchers alike. This trial marks empagliflozin as the first glucose-lowering agent to demonstrate a noticeable CV mortality risk reduction in patients with T2DM. Looking at the robust data, it is only a matter of time before there is a shift in the diabetes treatment paradigm.

The reference for this article is:
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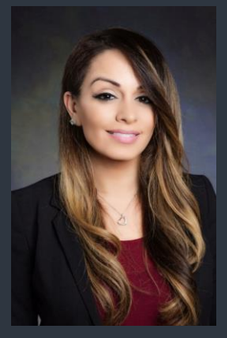
Melanie Stewart



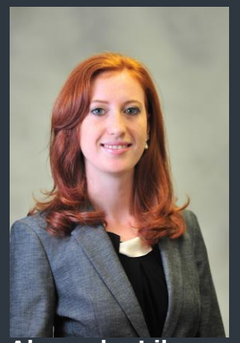
Parisa Karimi

Meet the Pharmacy Residents, Melanie Stewart and Parisa Karimi

Melanie Stewart is originally from Paramus, New Jersey. She earned a Doctor of Pharmacy degree in May 2015 from Rutgers University. Melanie is currently one of the PGY-1 resident pharmacists at The Valley Hospital, and her interests include oncology and infectious diseases. Her residency research project is focused on monitoring for increased incidence of side effects associated with a decreased infusion rate of bevacizumab in the outpatient infusion center. Melanie's career goals include practicing as a clinical pharmacy specialist, with plans to pursue a PGY2 residency in oncology or infectious diseases. In her free time, Dr. Stewart enjoys baking, singing, attending Broadway shows, and spending time with friends and family.

Parisa Karimi earned a Bachelor Degree in Risk Management from Georgia State University. Soon after she graduated with her business degree, she wanted to explore her interest in medicine and pursued her passion by attending pharmacy school. She graduated from Western University of Health Sciences in Southern California earning a Doctor of Pharmacy degree. Through her experiences, she developed skills in patient care, organizational infrastructure, and teamwork. Parisa is currently a PGY-1 resident pharmacist at The Valley Hospital. Her current interests are in emergency medicine and infectious diseases. After the completion of her residency, she plans on working in this capacity with a goal of obtaining certification as a Board Certified Pharmacotherapy Specialist.

Maria Leibfried



Alexandra Libman

Meet the Fairleigh Dickinson University School of Pharmacy Faculty, Maria Leibfried and Alexandra Libman

Maria Leibfried joined the FDU School of Pharmacy faculty in September 2015. As Clinical Assistant Professor of Pharmacy Practice based at The Valley Hospital, Maria provides Doctor of Pharmacy students with experiential education in internal medicine/acute care.

After earning a B.S. in Pharmacy and Doctor of Pharmacy from Rutgers University College of Pharmacy, Maria furthered her training through an ASHP-Accredited General Pharmacy Practice Residency at Montefiore Medical Center, Bronx, NY.

Maria's practice has included community pharmacy, hospital pharmacy, consultant pharmacy, and continuing education. Maria brought her years of practice into academia when she joined the faculty of St. John's University College of Pharmacy and Health Sciences in Queens, NY, and now has joined the School of Pharmacy at Fairleigh Dickinson University. In addition to being a licensed pharmacist in New Jersey and New York, she is Board Certified in Nutrition Support Pharmacy and is a Certified Consultant Pharmacist in NJ. Her research interests include asthma, cardiology, experiential education, geriatrics, informatics, inpatient pharmacy systems/performance improvement, interdisciplinary/interprofessional education, nutrition support, patient education, pedagogy, psychiatry.

Alexandra Libman (nickname: Sasha) joined the Fairleigh Dickinson University School of Pharmacy in August 2015. As Clinical Assistant Professor of Pharmacy Practice, Sasha precepts students during their experiential rotation in ambulatory care pharmacy practice at The Valley Hospital's Outpatient Heart Failure Clinic.

Sasha earned a Doctor of Pharmacy degree from Long Island University, Arnold & Marie Schwartz College of Pharmacy and Health Sciences in Brooklyn, NY. She completed an ASHP-accredited general pharmacy practice residency at Mount Sinai Beth Israel in New York, NY, and then continued on to do a second year of residency focused in geriatrics at the James J. Peters VA Medical Center in Bronx, NY. She successfully completed the Developing Excellence in Teaching for the Pharmacy Professional program at St. John's University College of Pharmacy and Health Sciences in Queens, NY. Sasha is a licensed pharmacist in the states of New York and New Jersey.

She enjoys educating students and inspiring them to develop as future leaders of pharmacy. Her interests include diabetes, hypertension, dyslipidemia, smoking cessation, asthma, COPD, and oncology.

Drug Info Corner

By: Maria Leibfried, BS, PharmD, BCNSP, CCP Pharmacist/FDU Faculty

Question:

Should Effient® be stopped in a patient that is to undergo dental surgery performed by a dental surgeon? If yes, when should it be stopped?

Answer:

Effient® (Prasugrel Tablets) is indicated to reduce the rate of thrombotic cardiovascular (CV) events in patients with acute coronary syndrome (ACS) who are managed with percutaneous coronary intervention (PCI). Prasugrel carries a Black Box Warning for bleeding risk, as it can cause significant, sometimes fatal, bleeding. [1]

CHEST guidelines (9th edition) and the package insert specify stopping prasugrel prior to coronary artery bypass graft. Other discontinuation guidelines, however, are not yet available.[1,2] The manufacturer recommends discontinuation of prasugrel for elective surgery, but does not specify when to stop the medication. In patients managed with PCI and stent, discontinuation of prasugrel, like other antiplatelets, increases the risk of stent thrombosis, myocardial infarction (MI), and death. Therefore, breaks in therapy should be avoided; if the medication is temporarily discontinued, it should be restarted as soon as possible.[1]

The American Dental Association recommends that it is not necessary for most patients to stop antiplatelet therapy before dental procedures, and that local measures be utilized to control bleeding. The risk of thrombotic events must be weighed against the risk of bleeding, and the potential to control bleeding with local measures, such as mechanical pressure, hemostatic agents, suturing, and tranexamic acid mouthwash. The patient's primary physician/cardiologist should be consulted. [3]

Napenas et al. retrospectively evaluated 29 patients who were on antiplatelet therapy and underwent 88 invasive dental procedure visits (extractions, periodontal surgery, subgingival scaling, root planing). The frequency of oral bleeding complications was so low that the risk of bleed was outweighed by the benefits of continuing antiplatelet therapy.[4]

A prospective study evaluated 129 patients on dual antiplatelet therapy (aspirin with either clopidogrel or prasugrel) that underwent tooth extraction. The authors concluded that, although bleeding time was longer in the patients on prasugrel, dental extraction can be safely performed in patients taking either clopidogrel or prasugrel.[5]

Summary

In most patients, the benefit of preventing thromboembolism, stroke, and MI with prasugrel therapy outweighs the risk of bleeding in patients undergoing dental procedures. Since bleeding time will be prolonged, additional measures to mitigate bleeding must be employed. Patient-specific decisions regarding prasugrel therapy should be made upon consultation with the primary physician/cardiologist

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2. Gordon H, Guyatt EA, Crowther M, et al. Executive Summary : Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines *Chest* 2012;141:7S-47S.
3. Ada.org. Anticoagulant and Antiplatelet Medications and Dental Procedures. 2015. Available at: http://www.ada.org/en/member-center/oral-health-topics/anticoagulant-antiplatelet-medications-and-dental-. Accessed 10/25/15.
4. Napenas J, Hong C, Brennan M, Furney S, Fox P, Lockhart P. The frequency of bleeding complications after invasive dental treatment in patients receiving single and dual antiplatelet therapy. *J Am Dent Assoc*. June 2009;140(6):690-5.
5. Prasugrel versus clopidogrel: a comparative examination of local bleeding after dental extraction in patients receiving dual antiplatelet therapy. *J Oral and Maxollofacial Surg*. Oct 2015;73(10):1894-1900.

P&T Committee: Formulary Additions

Trade/Generic Name: Entresto® (sacubitril/valsartan)

Drug Class: Angiotensin-receptor and neprilysin inhibitor

Formulation/Route of Administration: Oral tablets; sacubitril valsartan 24/26 mg, 49/51 mg, 97/103 mg

Indication: New York Heart Association (NYHA) class II to IV chronic heart failure and reduced fraction to reduce the risks for hospitalization for heart failure and cardiovascular death

Formulary Restrictions: None

Summary: Approval of Entresto™ was based on a double-blind trial (PARADIGM-HF) in 8442 patients with class II-IV heart failure and a reduced ejection fraction who were randomized to sacubitril 97 mg/valsartan 103 mg twice daily or the ACE inhibitor enalapril 10 mg twice daily, both in addition to other drugs. The study was stopped early because a pre-specified interim analysis showed lower cardiovascular mortality in patients randomized to sacubitril/valsartan. After a median follow-up of 27 months, the primary endpoint, a composite of first hospitalization for worsening heart failure or cardiovascular death, occurred in significantly fewer patients taking the combination compared to those taking enalapril (21.8% vs 26.5%). The combination significantly reduced the risk of first hospitalization for worsening heart failure (12.8% vs 15.6%), death from cardiovascular causes (13.3% vs 16.5%), and all-cause mortality (17.0% vs 19.8%). It also slowed the progression of heart failure.

Trade/Generic Name: Akynzeo® (netupitant/palonosetron)

Drug Class: Netupitant: substance p/neurokinin 1 (NK1) receptor antagonist

Palonosetron: serotonin-3 (5HT3) receptor antagonist

Formulation/Route of Administration: Oral capsule; netupitant 300 mg/ palonosetron 0.5mg

Indication: Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy

Formulary Restrictions: Restricted to Luckow infusion as a 6 month trial. Pharmacy will report back in 6 months

Summary: Chemotherapy induced nausea and vomiting (CINV) can significantly affect a patient's quality of life and lead to poor compliance with further chemotherapy treatment. The NCCN guidelines recommend that patients receiving highly emetogenic intravenous chemotherapy be treated with a corticosteroid in combination with a 5HT3 receptor antagonist and a neurokinin-1 receptor (NK1) antagonist. The combination of an oral-fixed dose combination of netupitant/palonosetron was designed to overcome potential barriers that prevented antiemetic guideline adherence by packaging guideline-recommended agents in a single oral-fixed dose. The approval of netupitant/palonosetron was based on the safety and efficacy demonstrated in pivotal clinical trials showing the netupitant/palonosetron offered superior prevention of CINV compared with palonosetron following highly emetogenic chemotherapy.

Preventing Nicotine Withdrawal and Supporting Smoking Cessation

By: Veronica Feltrin, FDU PharmD Candidate 2016
Alexandra Libman, PharmD, Pharmacist/FDU Faculty

According to the CDC, nicotine is the leading cause of drug addiction in the US. Nicotine, a naturally occurring substance found in tobacco, has been identified as being just as addicting as heroin, cocaine, and alcohol. Although many studies have shown numerous health benefits associated with smoking cessation, a large population in the US continues to struggle with nicotine addiction. Approximately 70% of current smokers have reported having an intention to quit smoking; since 2002, the amount of former smokers has surpassed the amount of current smokers. In order to continue this trend, The Valley Hospital is committed to making influential strides along with patients to combat nicotine withdrawal and addiction.

Nicotine withdrawal

It is important to prevent nicotine withdrawal in current smokers admitted to the hospital. As healthcare providers, it is our duty to ensure patients are given appropriate treatment modalities in lieu of smoking as withdrawal symptoms can complicate the primary reason for hospitalization. Symptoms of nicotine withdrawal are non-specific and may include irritability, anger, anxiety, difficulty thinking, increased hunger, and insomnia. Several treatment options are available for the prevention of these symptoms such as nicotine replacement products and non-nicotine agents. Dosing for these products is dependent on a patient's daily cigarette use; each cigarette contains approximately 2 mg of nicotine. Order sets are readily available in Meditech for patients who are current smokers. These order sets have a total of 4 treatment options, two nicotine containing agents and two non-nicotine containing agents. The nicotine containing agents include daily nicotine patches (24mg, 14 mg, and 7 mg) and nicotine gum (4 mg and 2 mg). The non-nicotine containing agents are Wellbutrin (buproprion) SR 150 mg and Chantix (varenicline) 0.5 mg tablets. For more information on how to navigate the order set, consult the pharmacist.

Smoking cessation

The Valley Hospital also offers smoking cessation group meetings for those patients that have made a decision to quit smoking. These meetings are held once a week, for a total of 6 consecutive weeks. This multidisciplinary meeting is led by a respiratory therapist, pharmacist, and case manager. Patients have the opportunity to, but are not forced to, express their current struggles and successes of becoming and staying smoke-free. Different therapies that are available to assist with this process are then discussed. At the end of each session, patients are given the option to take home one of two nicotine replacement agents (nicotine patch or nicotine gum) to assist them with their goal to quit smoking. These open sessions are especially helpful for those who are struggling with nicotine withdrawal, making the decision to quit smoking, or staying smoke free. If you would like to get involved or attend a session for general information, email Rowan Pragdat at rpragda@valleyhealth.com or Rebecca Bowlin at rbowlin@valleyhealth.com