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What's Inside This Issue?

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New Drug Updates

Delafloxacin (Baxdela™)

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In June of 2017, the U.S. Food and Drug Administration approved delafloxacin (Baxdela™) for the treatment of adults with acute bacterial skin and skin structure infections (ABSSI) caused by gram positive or negative bacteria, including methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*.[1] It is the newest medication in the fluoroquinolone antibiotic class and has a similar mechanism of action, in that it inhibits bacterial topoisomerase IV and DNA gyrase enzymes causing a disruption in the bacterial DNA replication, transcription, repair, and recombination.[2] Delafloxacin exhibits a concentration-dependent bactericidal activity against gram positive and gram negative bacteria in vitro.[2]

The efficacy of delafloxacin was demonstrated in two phase 3, multicenter, multinational, randomized, double-blinded, double-dummy non-inferiority trials in which patients with ABSSI were randomized to receive delafloxacin versus vancomycin plus aztreonam.[3] Trial 1 compared delafloxacin 300 mg intravenous infusion every 12 hours to the combination of intravenous vancomycin and aztreonam while Trial 2 compared delafloxacin 300 mg intravenous infusion every 12 hours for a total of 6 doses followed by a switch to oral delafloxacin 450 mg every 12 hours. The results of both trials indicated that intravenous and oral delafloxacin were non-inferior to the comparator in regards to clinical response, reduction in infection lesion size of at least 20%, achieved at the 48-72 hour endpoint (2-sided 95% CI for Trial 1 (-8.8, 3.6) for Trial 2 (-2.0, 8.3)).[3]
The most commonly reported side effects included nausea, diarrhea, headache, increased transaminases, and vomiting.

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Due to the pharmacological class of delafloxacin, a Black Box Warning exists for potentially irreversible serious reactions including tendinitis, tendon rupture, peripheral neuropathy, central nervous system effects, and exacerbation of Myasthenia Gravis.[2,3] Recommended prescribing information for the treatment of adults with ABSSI using delafloxacin is 300 mg injection every 12 hours over 60 minutes by intravenous infusion for 5-14 days or, 300 mg injection every 12 hours over 60 minutes by intravenous infusion ***then switch*** to 450 mg oral tablet every 12 hours at the discretion of a physician for a total of 5-14 days or, 450 mg oral tablets taken every 12 hours for 5-14 days.[3] The use of this medication is recommended for adults only and should not be used in pediatric patients. Patients with severe renal impairment (eGFR 15-29 mL/min/1.73m^2) should receive a dose adjustment for the injection formulation of 200 mg every 12 hours or 200 mg every 12 hours ***then switch*** to 450 mg oral tablet every 12 hours at the discretion of a physician. The use of delafloxacin in patients with ESRD is not recommended for both the injection and oral formulations. Physicians and pharmacists should counsel patients prescribed the oral formulation as it should be taken 2 hours before or 6 hours after any medications containing aluminum, magnesium, iron, or zinc as it will form a chelate.

References:

1. Voelker, Rebecca. Another Fluoroquinolone approved. *JAMA Network*. 2017; 318(5):416.
2. Baxdela® (delafloxacin) [prescribing information]. Lincolnshire, IL; Melinta Therapeutics, Incorporated; 2017
3. Drug Trials Snapshots: Baxdela. U.S. Food & Drug Administration website. https://www.fda.gov/Drugs/InformationOnDrugs/ucm565472.htm. Accessed 2017 Aug 16.

New Drugs Update for Cystic Fibrosis

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Cystic fibrosis (CF) is a genetic, progressive lung disease characterized by impaired mucociliary clearance, chronic endobronchial infections and airway obstruction.[1] The underlying cause is a gene mutation encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein, which consequently results in a defect or deficiency of CFTR activity. The CFTR protein is expressed in epithelial cells of various tissues throughout the body including the lungs, digestive tract, sweat glands, and genitourinary system. Thousands of CF-causing mutations have been identified, of which are further characterized into five classes according to pathological mechanisms.[2] While there is no cure for the disease, recent novel drug therapies targeting the CFTR protein have shown promising benefit for improvement in lung function.[3]

The first novel drug of its pharmacologic class, **Kalydeco™ (ivacaftor)**, was approved in 2012 as an orally bioavailable CFTR potentiator to increase the time that activated CFTR channels at the cell surface remain open.[4] In May 2017, the FDA expanded the indications of ivacaftor therapy with approval for use in 23 additional CF mutation variants from the original approval only in 10 specific CF-mutation variants.

Ivacaftor is now indicated for patients two years of age or older who have at least one mutation out of the 33 approved variations in the CFTR gene, even if solely based on in vitro data.[4] This expanded indication will potentially reach up to 900 CF patients who would not have had access to ivacaftor prior to May 2017. During phase III trials, ivacaftor demonstrated significant improvements in FEV1 even when added onto an existing regimen for CF treatment.[1] Ivacaftor was associated with more headache, upper respiratory tract infection, nasal congestion, rash, and dizziness compared to placebo though none of these led to discontinuation.[1] Ivacaftor is available as a 150 mg tablet dosed twice daily along with a fatty meal to increase absorption.[4]

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In the US, nearly half of CF patients have the homozygous allele for F508del CFTR protein mutation.[5] **Orkambi™ (lumacaftor/ivacaftor),** approved in 2015, is the first CF therapeutic that treats the disease itself, in comparison to the majority of CF therapies that only offer symptom management.[2] Lumacaftor is the first CFTR corrector that facilitates processing and trafficking of the F508del-CFTR protein to increase the amount at the epithelial cell surface, combined with a potentiator (ivacaftor). Phase III efficacy studies investigating lumacaftor-ivacaftor as an add-on to standard therapy in CF patients with F508del-CFTR are promising. The reported clinical outcomes favoring the novel drug compared to placebo include improvement of predicted FEV1 from baseline, less pulmonary exacerbations, and an overall lower rate of hospitalization and/or the use of intravenous antibiotics.[5,6] Efficacy and safety have not been established in patients with CF other than those homozygous for the F508del mutation.

This novel agent is approved for treatment of CF patients six years of age or older with the homozygous F508del-CFTR mutation. If patient genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene. Lumacaftor/ivacaftor is available as an oral combination (200/125 mg or 100/125 mg) tablet dosed twice daily. Adverse effects most commonly reported in studies include dyspnea, chest tightness, diarrhea, nausea, and nasopharyngitis. Dose reductions are warranted in patients with moderate or severe hepatic impairment and in patients concomitantly treated with strong CYP3A4 inhibitors.[7]

As with the majority of novel therapies, affordability is a major factor to consider. The data surrounding these two medications are encouraging, but the long-term benefits still require additional research. These novel agents expand the limited treatment options available for patients with cystic fibrosis, though their place in clinical practice has yet to be completely elucidated.

References

1) Gibson RL, Burns J.L, Ramsey B.W. Pathophysiology and management of pulmonary infections in cystic fibrosis. Am J Respir Crit Care Med. 168:918-51 (2003).
2) Schneider EK, Reyes-Ortega F, Li J, Velkov T. Can cystic fibrosis patients finally catch a breath with lumacaftor/ivacaftor? Clin Pharmacol Ther. 101: 130–141 (2017).
3) Ramsey, BW., et al. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. N Engl J Med. 365, 1663-1672 (2011).
4) KALYDECO™. [Package Insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; July 2017.
5) Wainwright, C.E., et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. N Engl J Med. 373, 220–231 (2015).
6) Brewington, J.J., McPhail, G.L. & Clancy, J.P. Lumacaftor alone and combined with ivacaftor: preclinical and clinical trial experience of F508del CFTR correction. Expert Rev Respir Med. 10, 5–17 (2016).
7) ORKAMBI™. [Package Insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; September 2016.

Call for Editors

The editors of *Pharmascript* are seeking content reviewers for upcoming editions. Interested Pharmacists, Residents and Students should contact Michael Armahizer (michaelarmahizer@umm.edu) or Vicki Leiman (victorialeiman@umm.edu). Reviewers should note specific areas of expertise or interest in their communications.

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Statistics Review

Sensitivity Vs Specificity

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Part of studying for the NAPLEX involves a begrudging review of biostatistics. A fair bit of that time is devoted to learning about the concepts of sensitivity, specificity, positive predictive value, and negative predictive value. These parameters are often used in conjunction to help critically evaluate diagnostic tools. Although, as pharmacists, our role tends not to fall in the area of diagnoses, with the increasing development and use of rapid diagnostic testing, it is essential that we understand both their strengths and limitations as these directly influence prescribing practices. As a quick recap:[1]

- Sensitivity is the probability of those with the disease testing positive for the disease of interest
- Specificity is the probability of those without the disease testing negative for the disease of interest

A practical and timely example of the importance of understanding these metrics is the use of rapid influenza diagnostic test (RIDT) kits. These RIDTs can be found in various practices settings, including pharmacies. The RIDTs are non-invasive, requiring only a nasal or throat swab, and can detect influenza A and/or B in a short amount of time. With results available in several hours, timely antiviral administration could assist in decreasing length and severity of symptoms. A recent systematic review compared the characteristics of common RIDTs, including sensitivity and specificity.[2] Focusing on Influenza A, the Sofia Immunoassay had a reported sensitivity of 93% (95% confidence interval 89 – 95%) and specificity of 95% (95% confidence interval 93 – 96%). For Alere I Influenza A, the sensitivity was reported as 97.9% (95% confidence interval 92.6 – 99.4%) and specificity as 86.2% (95% confidence interval 82.8 – 89%).

An important concept that the authors comment on, and is perhaps not as well understood, is that of positive and negative predictive values. [1]

- Positive predictive value (PPV) is the probability of those who tested positive actually having the disease of interest.
- Negative predictive value (NPV) is the probability of those who tested negative for the disease not actually having the disease of interest.

As clinicians, the PPV and NPV are what we would actually want to have available for assessment. It is important to understand that sensitivity and specificity are static values representative of the test itself, but PPV and NPV are also dependent on the prevalence of disease of interest. As such, PPV will be improved when the test is used in a population with high prevalence of the disease of interest.[3] For instance, we will discuss using the diagnostic test in symptomatic patients compared to those that do not have any symptoms, such as in a random sample. In the random sample you could expect, for instance, 100 patients to test positive, while only 20 may actually have the disease of interest (due to the smaller disease prevalence). If the test is limited to those with symptoms and a prior suspicion of disease (higher disease prevalence), 100 may test positive and 60 may have the disease of interest. Let's take the example of the above-mentioned RIDTs. If a RIDT has a reported sensitivity of 93%, meaning that 93% of the time those with influenza will test positive for influenza, and the overall prevalence of influenza in the population being tested is 15% the PPV will be approximately 76.7%. This translates to approximately 77% of patients that tested positive for influenza actually having influenza. Compare this to a population being tested that has an influenza prevalence of only 5%, the PPV goes down to roughly 50%. The number of false positive tests increases substantially, potentially resulting in unnecessary costs of care and treatment.

References

1. Motulsky H: **Intuitive Biostatistics**, Third Edition edn. New York, NY: Oxford University Press; 2014.
2. Koski RR and Klepser ME. A systematic review of rapid diagnostic tests for influenza: considerations for the community pharmacist. *J Am Pharm Assoc*. 57 (2017) 13e19
3. Hoppe C. Prevalence, sensitivity and positive predictive value. https://www.nature.com/nrn/journal/v14/n12/box/nrn3475-c5_BX1.html?foxtrotcallback=true&error=cookies_not_supported. Accessed 9.21.2017

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Practitioner Research Grant Winner Abstract for the 2015-2016 Academic Year

Re-initiation of Guideline-Directed Medical Therapy during Transitions of Care Following Cardiac Surgery

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Abstract:

Study Objective: To evaluate the impact of a post-discharge pharmacist-led intervention on outpatient re-initiation rates of select guideline-directed medical therapy in a cardiac surgery population, and to characterize the re-initiation rates at several time periods throughout transitions of care.

Design: Prospective quasi-experimental (pre-post intervention) cohort study.

Intervention: Patients enrolled February 12, 2016 through October 4, 2016 were placed in the control group, while patients enrolled October 5, 2016 through March 1, 2017 were placed in the intervention group. In the intervention group, if the study medication was not re-initiated prior to the cardiac surgeon visit, a paper intervention form was placed in the paper medical chart for review and completion by the cardiac surgeon at the time of outpatient follow-up visit.

Setting: Adult patients undergoing cardiac surgery at a large academic medical center.

Patients: Two hundred forty-five adults admitted for cardiac surgery who were prescribed a beta blocker, angiotensin-II converting enzyme inhibitor (ACE-I) or angiotensin-II receptor blocker (ARB) prior to admission for the management of at least one select compelling indication.

Results: Intervention forms were returned for 29.4% of patients in the intervention group. Post-discharge pharmacist intervention resulted in a trend towards an increase in ACE-I and ARB re-initiation rates at the first cardiac surgeon outpatient follow-up visit when compared to the control group (24.5% vs. 7.5%, $p = 0.053$). The discharge re-initiation rate was significantly lower for ACE-Is and ARBs when compared to beta blockers (26.6% vs. 94.6%, $p < 0.001$). Cumulative re-initiation rates of ACE-Is or ARBs at the cardiac surgeon follow-up visit and at six months post-discharge were 44.2% and 65.5%, respectively. Of patients prescribed ACE-Is or ARBs prior to admission without re-initiation at discharge, 30.2% had no documented relative contraindication to re-initiation. Of patients prescribed ACE-Is or ARBs prior to admission without re-initiation at the cardiac surgeon follow-up visit, 63.5% had no documented relative contraindication to re-initiation.

Conclusion: Pharmacist-led intervention in the post-discharge period resulted in a 16% increase in the re-initiation rate of ACE-Is and ARBs. The discharge re-initiation rate for ACE-Is and ARBs was significantly lower than for beta blockers. At the end of the six month follow-up period, approximately one-third of patients prescribed an ACE-I or ARB prior to admission had not been re-initiated. Many relative contraindications resolved in the post-discharge period, indicating an opportunity for intervention to improve re-initiation rates. Additional strategies to increase post-discharge re-initiation of ACE-Is or ARBs should be explored, including increasing the involvement of outpatient cardiologists.

Deadlines for Upcoming Pharmascript Editions

December 15, 2017 for publication in the January 2018 edition
March 16, 2018 for publication in the April 2018 edition
June 15, 2018 for publication in the July 2018 edition
September 21, 2018 for publication in the October 2018 edition

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Vaccination Update

Changes to the HPV Vaccination Schedule

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In December 2016 the Advisory Committee on Immunization Practices (ACIP), revised the recommended schedule for routine immunization for the Human Papilloma Virus (HPV). While originally approved as a three-dose series given over six months, now teens fourteen years old and under will be considered fully vaccinated after two doses, as long as those doses are administered at least five months apart (1).

The schedule change is based on immunogenicity studies that showed that two vaccine doses lead to a strong immune response in younger adolescents (≤ 14 years). For all older adolescents, the vaccine series consists of three doses; the initial dose, a second two months later and a third at least six months after that (Table 1)(1).

Initiating Age	Dose	Schedule	Interval
Starting at 9 through 14 years, except if immunocompromised	2 doses	1st dose – 0 2nd dose - 6 to 12 months	At least 5 months between doses
Starting 15 to 26 years, or immunocompromised at any age	3 doses	1st dose - 0 2nd dose -1 to 2 months 3rd dose - 6 months	Between doses 1 and 2 = 4 weeks Between doses 2 and 3 = 12 weeks Between doses 1 and 3 = 5 months

Table 1. ACIP recommendations for Human Papilloma Virus (HPV) vaccination doses and schedule by age at initiation and medical conditions (1)

HPV is the most common sexually transmitted disease in the U.S. and the Centers for Disease Control (CDC) estimate 14 million new infections in Americans annually (2). The link between HPV infection and cervical cancer in women is long established, but HPV infections also lead to oropharyngeal as well as anal and rectal cancers in both sexes. The CDC estimates that each year HPV infections cause 19,400 cancer cases in women and 12,100 in men and up to 90% could be prevented by HPV vaccination(3).

The HPV vaccine is a routine immunization recommended for adolescent boys and girls ages 11 and 12. For those not vaccinated, catch-up vaccinations for females through age 26 and males through age 21 are recommended. Vaccination is also recommended through age 26 for men who have sex with men or who are immunocompromised (1). Currently there is one HPV vaccine available in the U.S., GARDASIL® 9 (Merck & Co.,Inc.). It contains antigens to HPV-16 and HPV-18, the most common oncogenic HPV strains, as well as antigens to five other, less prevalent, HPV strains. Additionally, GARDASIL® 9 has antigens to HPV-6 and HPV-11 that cause genital warts. While the prior formulation (Gardasil®, Merck & Co.,Inc.) contained only four HPV antigens, there is no ACIP recommendation on additional vaccination for those who completed the series with another formulation. Adolescents or adults who started the vaccine series with previous formulations, can complete the series with GARDASIL® 9 (1).

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The side effects of HPV vaccination are often mild, including pain and swelling at the injection site or headache and pyrexia (4). For women, cervical cancer screening remains an important method for cancer prevention. Routine cervical cancer screening is still recommended for both vaccinated and un-vaccinated women.

Outcomes data has shown a decrease in HPV infections in U.S. teens since the introduction of the first HPV vaccine ten years ago. However, nationwide, few young people are fully vaccinated against HPV. In Maryland, 2016 estimates are that 44.5 (±9.1)% of boys and 51.8 (±9.2)% of girls completed the three dose series (5).

Pharmacists have a role in improving HPV vaccination rates. Maryland pharmacists are authorized to administer the HPV vaccine to adolescents 11 to 17 years old with a prescription and to those 18 and older under a protocol. Pharmacists, as a part of the care team, are well placed to answer parent and patient questions about the vaccine and to identify those who have started the series and encourage them to receive the final doses.

Detailed information about the HPV vaccine, its administration and contraindications can be obtained from the CDC. Information for parents and teens about the vaccine is available from organizations like the CDC, immunize.org or the American Academy of Pediatrics.

1) Meites E, Kempe A, Markowitz LE. Use of a 2-Dose Schedule for Human Papillomavirus Vaccination — Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep 2016;65:1405–1408.
2) Centers for Disease Control and Prevention. Epidemiology and Prevention of Vaccine-Preventable Diseases. Hamborsky J, Kroger A, Wolfe S, eds. 13th ed. Washington D.C. Public Health Foundation, 2015.
3) Centers for Disease Control and Prevention, Division of Cancer Prevention and Control. "How Many Cancers Are Linked with HPV Each Year?" https://www.cdc.gov/cancer/hpv/statistics/cases.htm. March 3, 2017. Accessed May 10, 2017.
4) GARDASIL® 9. Injection prescribing information. Whitehouse Station, NJ: Merck & Co., Inc.; October 2016.
5) Walker TY, Elam-Evans LD, Singleton JA, et al. National, Regional, State, and Selected Local Area Vaccination Coverage Among Adolescents Aged 13–17 Years — United States, 2016. MMWR Morb Mortal Wkly Rep 2017;66:874–882.

Clinical Review

Angiotensin II for the Treatment of Vasodilatory Shock: A clinical review of a recent publication

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Vasodilatory shock, the most common type of shock, is caused by excessively relaxed blood vessels, leading to peripheral vasodilation and hypotension, despite preserved cardiac output. Immediate reestablishment of blood pressure, initially using fluid resuscitation, followed by catecholamines and vasopressin, if necessary, is required to ensure organ perfusion.[1] Persistent hypotension after vasopressor initiation leads to a dramatically decreased chance of survival.

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The New England Journal of Medicine recently published a study that sought to investigate the effectiveness of angiotensin II for the treatment of resistant vasodilatory shock. The trial was an international, randomized, placebo-controlled trial where a total of 321 patients received one of two regimens: 163 patients received angiotensin II and 158 received placebo. Baseline characteristics were not significantly different between the two groups; patients in both study arms were critically ill (as indicated by high APACHE II scores, with a median score of 28 corresponding to 55% mortality rate), had increased baseline vasopressor doses, and had sepsis as the most common cause of shock (80.7%). Eligible patients were 18 years of age or older and had vasodilatory shock, defined as a cardiac index greater than 2.3 L/min/m^2 or as a central venous oxygen saturation of greater than 70% in conjunction with central venous pressure of more 8 mm Hg, with a mean arterial pressure (MAP) between 55 and 70 mm Hg, despite IV volume resuscitation with at least 25 mL/kg over the previous 24 hours and the administration of high dose vasopressors. High dose vasopressors were defined as more than 0.2 mcg/kg/min of norepinephrine, or the equivalent dose of another vasopressor, for a minimum of 6 hours and a maximum of 48 hours. The inclusion and exclusion criteria can be found in Table 1. Angiotensin II was initiated at 20 ng/kg/min and titrated within the first 3 hours to attain a MAP of at least 75 mm Hg and continued for up to 48 hours. The primary endpoint was MAP response at 3 hours after start of the study infusion (MAP $\geq$ 75 mm Hg or an increase $\geq$ 10 mm Hg from baseline).

Approximately 70 percent of patients in the angiotensin group versus 23 percent of patients in the placebo group met the criteria for the primary efficacy endpoint of MAP response (69.9% vs. 23.4%, $p<0.001$). Secondary outcomes included changes in the cardiovascular SOFA score and the total SOFA score between baseline measurement and hour 48. The results of the end points are summarized in Table 2.

An adverse event was reported in 87.1% of patients receiving angiotensin II and 91.8% of patients who received placebo. Discontinuation of the study drug or placebo due to an adverse event, most commonly septic shock, multiorgan failure, cardiogenic shock, and cardiac arrest, occurred in 14.1% and 21.5% of patients, respectively.

Unfortunately, treatment for resistant vasodilatory shock is sparse. Available treatments include glucocorticoids, vasopressin, methylene blue and high volume hemofiltration, all of which are associated with adverse events. Although angiotensin II, in this study, was not coupled with increased mortality or adverse events, the role of angiotensin II for vasodilatory shock remains unclear. Patients who received angiotensin II met the primary endpoint more frequently than those who received placebo, but the mean change in vasopressor dose was minimal (-0.03 $\pm$ 0.10 versus +0.03 $\pm$ 0.23) and the mortality was not significantly decreased. Future studies should evaluate whether or not a mortality benefit exists with angiotensin II.

Limitations of this study include a relatively small sample size (potential side effects of angiotensin II may not have been identified), and a limited follow up period of 28 days (long term effects of angiotensin still remain to be determined). As patients with cardiogenic shock were excluded, the safety and efficacy of angiotensin II remains unknown in this population. Moreover, as angiotensin II increased the MAP, and therefore decreased doses of background vasopressors, clinicians may have become “un-blinded” and have been able to predict the treatment groups. Another critique of this study is the definition of high dose vasopressors, which in this study was defined as greater than 0.2 mcg/kg/min of norepinephrine or the equivalent. While no standard threshold exists, this is a relatively low threshold to initiate a second line vasopressive agent.

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In conclusion, angiotensin II increases blood pressure and allows dose reductions in catecholamines in patients with resistant vasodilatory shock, but the long-term effects, mortality benefit, and comparison to other vasopressors remain unknown.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria:	**Exclusion Criteria:**
-18 years of age and older and had vasodilatory shock despite IV volume resuscitation with at least 25 mL/kg of body weight over the previous 24 hours and the administration of high dose vasopressors -Indwelling bladder catheter and arterial catheter	-Patients who had burns covering more than 20% of the total BSA, acute coronary syndrome, bronchospasm, liver failure, mesenteric ischemia, active bleeding, abdominal aortic aneurism, an absolute neutrophil count <1000/mm^3, or who were receiving venoarterial extracorporeal membrane oxygenation or treatment with high dose glucocorticoids

Table 2: Summary of End Points

End Point	**Angiotensin II (N = 163)**	**Placebo (N = 158)**	**Odds or Hazards Ration (95% CI)**	**P Value**
Primary end point				
MAP response at hour 3, n (%)	114 (69.9)	37 (23.4)	Odds ratio, 7.95 (4.76-13.3)	<0.001
Secondary end points				
Mean change in cardiovascular SOFA score at hour 48	-1.75 $\pm$ 1.77	-1.28 $\pm$ 1.65		0.01
Mean change in total SOFA score at hour 48	1.05 $\pm$ 5.50	1.04 $\pm$ 5.34		0.49
Additional end points				
Mean change in norepinephrine-equivalent dose from baseline to hour 3 (mcg/kg/min)	-0.03 $\pm$ 0.10	0.03 $\pm$ 0.23		<0.001
All-cause mortality at day 7 n (%)	47 (29)	55 (35)	Hazard ratio, 0.78 (0.53-1.16)	0.22
All cause mortality at day 28 n (%)	75 (46)	85 (54)	Hazard ratio, 0.78 (0.57-1.07)	0.12

References:

1) Khanna A, English S, Wang X, et al. Angiotensin II for the Treatment of Vasodilatory Shock. N Engl J Med. 2017 Aug 3; 377:419-430.

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Developing Pharmacy Leaders: Student Leadership Workshop

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For the third year, The Johns Hopkins Summer Internship Program in conjunction with Maryland Society of Health-System Pharmacists sponsored a Student Leadership Workshop (SLW). On Saturday, July 8th 2017, students from schools of pharmacy from across the nation gathered at The Johns Hopkins Hospital in Baltimore, Maryland to attend the SLW.

The all-day program included presentations by local pharmacist leaders, including:

- Dean Anne Lin, PharmD, FNAP, Notre Dame of Maryland University
- Dr. Kristin Watson, PharmD, BCPS-AQ Cardiology, University of Maryland School of Pharmacy
- Dr. John Lindsley, PharmD, BCPS-AQ Cardiology, The Johns Hopkins Hospital
- Mr. Daniel Ashby, MS, FASHP, The Johns Hopkins Hospital
- Dr. Stacy Dalpoas, PharmD, BCPS, The Johns Hopkins Bayview Medical Center

In the morning, students learned about leadership styles from Dean Lin and skills to strive towards work-life balance from Dr. Watson. Dr. Lindsley shared real life stories and tips in preparation for Advanced Pharmacy Practice Experiences. In the afternoon, students had the opportunity to share their own individual leadership activities in a collaborative poster presentation and identify opportunities to develop new pharmacy programs for their own school communities. Mr. Ashby discussed emotional intelligence and mentorship and Dr. Dalpoas ended the workshop by leading discussions on developing curriculum vitae in preparation for residencies.

Students enjoyed the event, commenting “The residency and CV info was very informative on things I didn’t know yet, and the student posters helped me network!”, “I thought the speakers were incredibly engaging and the topics were extremely relevant”, and “I enjoyed the tips and advice on residency applications and APPEs. These topics are on the mind of third year pharmacy students (which made up the large portion of those in attendance).”

For more information about next year’s program, please check back in the spring of 2018.

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Photographs from this year’s workshop:

Break time between speakers

Breakout group discussions

Student leadership activity poster presentations