THE LOBBYIST

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DISTRICT OF COLUMBIA COLLEGE OF CLINICAL PHARMACY

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PRESIDENT'S LETTER

Dear Colleagues,

As the current year is quickly approaching an end, I would like to provide everyone with some updates on our executive board and past/upcoming events.

First and foremost, I would like to extend a warm welcome to our new President-Elect, Memar Ayalew. Dr. Ayalew is an Infectious Diseases Clinical Pharmacist at Walter Reed National Military Medical Center. She led the effort in starting the Antimicrobial Stewardship Program at the facility that is currently thriving and provides pharmacy services for the adult infectious diseases consult team. Dr. Ayalew completed her B.S. in Biology at the University of the District of Columbia, and her PharmD at the University of Maryland Eastern Shore School of Pharmacy. Her ASHP-accredited Acute Care Pharmacy Practice Residency was fulfilled at Novant Health Forsyth Medical Center. She currently serves as a co-chair of the Antimicrobial Stewardship Committee and a member of the Infection Control Committee. She is also an active member of ASHP, SIDP and ACCP. Please join me in welcoming Dr. Ayalew to DC-CCP.

In April, DC-CCP members collaborated on Capitol Hill and participated in the annual Advocacy Day. About 40 students attended from UMD, Shenandoah, and VCU. Participants met with offices of Senators from Maryland, VA, PA, and WV as well as Rep. Comstock who represents the Winchester area. It was a great success on a beautiful day!

In September, a networking/social event was held at Nationals Park as DC-CCP members attended a Nationals vs. Brewers game together.

Our pharmacist networking & education committee has been diligently planning the Fall CE Forum, which is scheduled for October 13, 2018 from 8am-1pm at Holy Cross Hospital in Silver Spring, MD. I encourage all members to register for this 3-CE opportunity and spread the word to your colleagues.

Stay tuned for more upcoming networking/social events and award nominations as our year comes to an end.

Chelsea McSwain, Pharm.D., BCPS, BCCCP
DC-CCP President

MEMBER SPOTLIGHT

Erin VanMeter, PharmD, BCACP

Assistant Professor; Ambulatory Care Pharmacy Specialist

In this edition of The Lobbyist, we would like to feature Dr. Erin VanMeter who is currently DC-CCP's committee chair for the networking and education committee. She was most recently involved in coordinating and presenting at DC-CCP's Fall 2018 CE Forum.

Dr. VanMeter received her Doctor of Pharmacy degree from Shenandoah University Bernard J Dunn School of Pharmacy. Dr. VanMeter completed her PGY1 Pharmacy Practice Residency at the Martinsburg Veterans Affairs Hospital in Martinsburg, WV, and her PGY2 Ambulatory Care Residency at the VA Maryland Health Care System in Baltimore, MD. After completion of her residency, Dr. VanMeter took a position with The Ohio State University Wexner Medical Center, where she practiced in an anticoagulation clinic and implemented clinical ambulatory care pharmacy services in a physician-owned primary care group. She joined The University of Maryland School of Pharmacy in October2017 as an Assistant Professor in the Department of Pharmacy Practice and Science. Dr. VanMeter practices as an Ambulatory Care Clinical Pharmacy Specialist at multiple Johns Hopkins Community Physician sites in the Greater Washington region and the Interprofessoinal Care Transitions Clinic at University of Maryland Prince George's Hospital. Her research interest includes clinical outcomes in chronic disease management, practice-based research, patient counseling and education, vulnerable populations, and interprofessional education. Thank you for your dedication to the organization and the pharmacy profession!

Dr. VanMeter presenting on updates in Diabetes type II Management at DC-CCP's Fall 2018 CE Forum Event

New DC-CCP Officer

Please join us in welcoming Dr. Memar Ayalew as DC-CCP's new President Elect. Dr. Ayalew received her Doctor of Pharmacy from the University of Maryland Eastern Shore School of Pharmacy and completed her PGY-1 at Novant Health Forsyth Medical Center. She is currently practicing as an Infectious Diseases Clinical Pharmacist at Walter Reed National Military Medical Center and has led the effort in starting the Antimicrobial Stewardship Program.

DC-CCP Fall 2018 CE Forum Event Update

On October 13th, DC-CCP hosted their annual fall CE Forum event at Holy Cross Hospital. Presentation topics included "The Impact of Medications on Wound Healing," "Diabetes Management: What's New with Type II," and "Pharmacy Perioperative Care related to Enhanced Recovery Program." It was a privilege to have our guest speakers Dr. Jessica Pyhtila, Dr. Erin VanMeter, and Dr. Richard Parrish share their knowledge and experience in these topics.

The program also included a residency round table event for the pharmacy students who attended. Students were able to hear about previous pharmacists' residency experiences and get better insight into how to prepare for residency.

New Drug Update: Tezacaftor/Ivacaftor (SYMDEKO®)

Ankit Gandhi, PharmD Candidate 2019[1]; Charles Summerlin, PharmD Candidate 2019[1]; and Kimberly Durand, PharmD[2]

[1]University of Maryland School of Pharmacy

[2]The Johns Hopkins Hospital

Cystic fibrosis (CF) is an inherited autosomal recessive genetic disease resulting in a mutation of the cystic fibrosis transmembrane conductance regulator (*CFTR*) protein. The *CFTR* protein is a chloride transporter commonly found on epithelial cells and allows for passage of chloride ions, thereby regulating the movement of sodium and water. This genetic disorder results in the formation of thick mucus that obstructs passageways in the lungs, pancreas, and other organs. The resulting complications lead to progressive lung damage as well as frequent respiratory infections that are often multi-drug resistant.

In February of 2018, the Food and Drug Administration (FDA) approved tezacaftor/ivacaftor (SYMDEKO®) for the treatment of patients with CF aged 12 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the *CFTR* gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence.

Image retrieved from: http://www.empr.com/Symdeko/drug/34796/

Mechanism of Action

SYMDEKO® is a combination of tezacaftor and ivacaftor. Tezacaftor facilitates the movement of the defective *CFTR* protein to the cell surface. Ivacaftor is a *CFTR* potentiator that helps facilitate the opening of the chloride channel on the cell surface to increase chloride transport. The combined effect of tezacaftor and ivacaftor is increased quantity and function of *CFTR* at the cell surface, which results in increased chloride transport.

Clinical Evidence

Approval of SYMDEKO® was granted based on evidence from three Phase 3, double-blind, and placebo-controlled clinical trials that included a total of 916 patients with CF, as summarized below in Table 1.

Table 1: Summary of Clinical Evidence

	EVOLVE (Trial 1)	EXPAND (Trial 2)	EXTEND (Trial 3)
Patient Population	Patients with CF aged 12 years and older who were homozygous for the *F508del* mutation	Patients with CF aged 12 years and older who were heterozygous for the *F508del* mutation and a second *CFTR* mutation* that was predicted to be responsive to SYMDEKO® therapy	Patients with CF aged 12 years and older who were heterozygous for the *F508del* mutation and a second *CFTR* mutation† that was predicted to be unresponsive to SYMDEKO® therapy
Study Design	Phase 3, 24-week, randomized, double-blind, placebo-controlled, two-arm study	Phase 3, 8-week, randomized, double-blind, placebo-controlled, 2-period, 3-treatment crossover study	Phase 3, 12-week randomized, double-blind, placebo-controlled, two-arm study
Number of Patients	504 patients (248 SYMDEKO®, 256 placebo)	244 patients (161 SYMDEKO®, 156 ivacaftor [KALYDECO®], 161 placebo)	168 patients (83 SYMDEKO®, 85 placebo)
Results of Primary Efficacy Endpoints	4% improvement versus placebo in mean absolute change in ppFEV1, from baseline through 24 months (95% CI: 3.1, 4.8; P<0.0001)	6.8% improvement versus placebo in mean absolute change in ppFEV1, from baseline to the average of weeks 4 and 8 (95% CI: 5.7, 7.8; P<0.0001). 2.1% improvement versus ivacaftor (KALYDECO®) in mean absolute change in ppFEV1, from baseline to the average of weeks 4 and 8 (95% CI: 5.7, 7.8; P<0.0001).	1.2% improvement versus placebo in mean absolute change in ppFEV1, from baseline through week 12. Study was terminated following the planned interim analysis because the pre-specified futility criteria were met.

ppFEV1 = percent predicted forced expiratory volume in one second

** = mutations predicted to be responsive were selected for the study based on the clinical phenotype (pancreatic sufficiency), biomarker data (sweat chloride), and in vitro responsiveness to tezacaftor/ivacaftor*

† = Mutations predicted to be non-responsive were selected for the study based on biologic plausibility (mutation class), clinical phenotype (pancreatic insufficiency), biomarker data (sweat chloride), and in vitro testing to tezacaftor and/or ivacaftor.

Side Effects & Administration

The most commonly reported side effects of SYMDEKO® based on the clinical trials are: headache, nasopharyngitis, nausea, sinus congestion, and dizziness. Serious side effects include transaminase elevations and cataracts.

SYMDEKO® is supplied as a tablet for oral administration. The recommended dosage is one tablet (tezacaftor 100mg/ivacaftor 150mg) by mouth in the morning and one tablet (ivacaftor 150mg) by mouth in the evening, approximately 12 hours apart. SYMDEKO® needs a dose adjustment in patients with hepatic impairment or in those patients who are taking other drugs that are CYP3A inhibitors. Patients are instructed to swallow the tablets whole and to take the medication with fat-containing foods.

Place in Therapy and Conclusions

In summary, SYMDEKO® is an excellent new therapy option for patients with cystic fibrosis, particularly in patients who either never started or discontinued ORKAMBI® (lumacaftor/ivacaftor). SYMDEKO® has fewer side effects in comparison to ORKAMBI®, which has similar side effects as to that of SYMDEKO® in addition to chest discomfort, dyspnea, and an increase in blood pressure. ORKAMBI® is also only used for patients that are homozygous for the *F508del* mutation, whereas SYMDEKO® can be an option for patients that are heterozygous as well. One disadvantage is that SYMDEKO® is currently only approved for patients aged 12 years and older while ORKAMBI® is approved for patients aged 2 years and older. However, Vertex Pharmaceuticals is expected to release results later this year from a phase 3 study evaluating SYMDEKO® in patients aged 6 through 11 years, which could potentially result in an expansion of the drug's approval to include use in this younger patient population.

References:

1. Drug Trials Snapshots: SYMDEKO®. U.S. Food and Drug Administration. https://www.fda.gov/Drugs/InformationOnDrugs/ucm598699.htm. Updated March 2018. Accessed July 2018.
2. SYMDEKO® [Prescribing Information]. Boston, MA: Vertex Pharmaceuticals; 2018.

Review of the Valsartan 2018 Recall

AhnThu Tran, PharmD Candidate 2019, Shenandoah University School of Pharmacy

The FDA announced a list of valsartan products under recall in July 2018 due to contamination with N-nitrosodiumethylamine (NMDA). In animal studies, NDMA increased the occurrence of cancer using amounts of NDMA much higher than levels in the recalled valsartan batches.[1] Consuming up to 96ng NDMA per day is considered reasonably safe for human ingestion and can be found in some water supplies and food. Throughout a person's lifetime, consuming this amount of NDMA would result in less than one additional case of cancer for every 100,000 people.[1] The amounts of NDMA in the recalled batches of valsartan exceeded the acceptable levels and some levels of the impurity may have been in the valsartan containing products for as long as four years.

The initial recalled products were found to be manufactured by Zhejiang Huahai Pharmaceuticals in China. FDA has also contacted other manufacturers to assess if their processes are at risk and to prevent future valsartan products contamination with NDMA.

The following are the current manufacturers that are on the list of recalls; more details of the manufacturers are available on the FDA website:[1]

- Teva Pharmaceuticals labeled as Major Pharmaceuticals
- Teva Pharmaceuticals USA labeled as Actavis
- Prinston Pharmaceutical Inc. labeled as Solco Healthcare LLC.
- AvKARE
- Remedy Repack
- A-S Medication Solutions LLC
- Bryant Ranch Prepack Inc.
- H.J. Harkins Company Inc. dba Pharma Pac
- Proficient Rx LP
- Northwind Pharmaceuticals
- Camber Pharmaceuticals Inc.
- NuCare Pharmaceuticals Inc.

Valsartan is an angiotensin receptor blocker (ARB) indicated for the treatment of hypertension and has been shown to reduce morbidity and mortality in patients with heart failure with reduced ejection fraction. Thus, it is important for patients to continue therapy. Patients can be switched another valsartan product that is not in the list of recall or a different ARB or angiotensin converting enzyme inhibitor (ACEi).

Angiotensin Receptor Blockers therapeutic interchange[2]				
Candesartan (Atacand)	4 mg daily	8 mg daily or divided BID	16 mg daily or divided BID	16 mg daily or divided BID to 32 mg daily or divided BID
Irbesartan (Avapro)	75 mg daily	150 mg daily	300 mg daily	300 mg daily
Losartan (Cozaar)	25 mg daily	50 mg daily or divided BID	100 mg daily	- - - -
Olmesartan (Benicar)	10 mg daily	20 mg daily	20 mg daily to 40 mg daily	40 mg daily
Telmisartan (Micardis)	20 mg daily	40 mg daily	40 mg daily to 80 mg daily	80 mg daily
Valsartan (Diovan)	40 mg daily or 20 mg BID	80 mg daily or 40 mg BID	160 mg daily	320 mg daily

References:

1. FDA updates on valsartan recalls. FDA U.S. Food & Drug Administration. (www.fda.gov/drugs/drugsafety/ucm613916.htm). Written: 4 August 2018. Accessed 13 August 2018.
2. Angiotensin receptor blocker (ARB) antihypertensive dose comparison. Pharmacist's Letter/Prescriber's Letter 2009 (Full update February 2012); 25(8):250801.

New Treatment of Hereditary Transthyretin-mediate Amyloidosis: Onpattaro™

Sierra Simpkins, PharmD Candidate 2019, University of Maryland School of Pharmacy

Hereditary transthyretin-mediated amyloidosis (hATTR) is a rare autosomal dominant disease that affects approximately 50,000 people worldwide.[1,2] hATTR is caused by a mutation in transthyretin (TTR) protein, which is produced in the liver, resulting in amyloid deposits that the heart, nerves, and GI tract.[2] Presentations of hATTR include polyneuropathy and cardioneuropathy.[2] As the protein deposits accumulate, symptomatic presentation can range from loss of sensation to abnormal involuntary bodily functions. Specific symptoms may include severe constipation, proteinuria, carpal tunnel syndrome, progressive dementia, organ failure, numbness, and tingling.[3]

Traditional treatment of hATTR primarily focuses on symptom management coordinated by an amyloidosis specialist. Active treatment options include liver transplant and use of protein tetramer stabilizers. For a small subset of patients,

orthotopic liver transplant is an option for improving survival but excludes persons of older age, prior comorbidity diagnosis, and advanced hATTR disease.[1] TTR protein tetramer stabilizers help prevent dissociation of protein monomers but have no impact on the synthesis of the mutated protein.[1] Neither liver transplant nor the use of TTR stabilizers permanently halts disease progression.[1]

The progressive nature of the disease and the limitations of the current treatments options demonstrate the need for additional therapeutic interventions for symptomatic management of hATTR.

First Approved RNA Interference Gene Silencer

In August 2018, the Food and Drug Administration approved Alnylam Pharmaceutical's patisiran (Onpattro™), the first agent in the small interfering ribonucleic acid (siRNA) drug class, indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.[4,5] Onpattro™ uses a lipid nanoparticle to encase the siRNA, allowing for drug delivery directed to the liver.[4] At the site-of-action, the double-stranded siRNA causes degradation of the mutated and wild-type TTR mRNA via RNA interference.[5] Onpattro™ requires intravenous infusion once every three weeks for the duration of the patient's life.[5,6]

The APOLLO trial demonstrated the efficacy of Onpattro.[4] A randomized, double-blind, placebo-controlled, multicenter clinical trial of 225 adult patients with polyneuropathy caused by hATTR amyloidosis.[4,5] All patients received premedication with a corticosteroid, acetaminophen, H1, and H2 blockers prior to infusion every three weeks for 18 months.[5] The primary endpoint was the change in the modified Neuropathy Impairment Score +7 (mNIS+7) compared to baseline.[5] The secondary endopoint evaluated quality of life based on the Norfolk Quality of Life-Diabetic Neuropathy (QoL-DN).[5] In this trial, comparing Onpattro to placebo, the treatment difference, LS mean for mNIS+7: -34 (95% CI: -39.9, -28) and for the Norfolk QoL-DN: -21.1 (95% CI: -27.2, -15.0).[5] A decrease in mNIS+7 and Norfolk QoL-DN indicates improvement. Due to the rare presentation of hATTR amyloidosis the scope of these findings were based on a sample size of 148 participants in the treatment group compared to 77 participants in the placebo group.

The most common side effects (>10%) in Onpattro treated patients were upper respiratory infections and infusion-related reactions.[5] Other side effects (>5%) in Onpattro treated patients included dyspepsia, dyspnea, muscle spasm, arthralgia, erythema, bronchitis, and vertigo.[5] Due to inhibiting production of TRR, patients receiving Onpattro therapy may experience Vitamin A deficiency and therefore supplementation is recommended. Providers must counsel patients on reporting ocular symptoms, such as night blindness immediately.[5]

Cost of Onpattro Therapy

As a life-long, weight-based treatment option, experts are projecting Onpattro to cost, $450,000 per patient per year.[7] In efforts to increase patient access to Onpattro, Alnylam appears to be taking steps to provide a "money back guarantee" for insurers.[7]

Conclusion

hATTR is a progressive disease that significantly impacts quality of life and shortens life expectancy. Based on the efficacy in reducing symptoms of neuropathy in clinical trials, the approval of Onpattro has provided a treatment option that appears promising in improving quality of life for individuals living with hATTR. With the ability to halt TTR production, Onpattro may also prove to have an impact on disease progression in future clinical trials. With its success and monumental impact on hATTR, Onpattro is paving the way for gene silencing therapy.

References:

1. Hereditary ATTR amyloidosis: a progressive and life-threatening familial disease1-3 [Internet]. Hereditary ATTR Amyloidosis and Mechanism of Disease. [cited 2018Aug22]. Available from: https://www.hattramyloidosis.com/diseasebackground?gclid=EAIaIQobChMIof2L2Zv-3AIVTVmGCh3wPQiQEAAYASAAEgI8OfD_BwE.
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4. Alnylam's Onpattro is the first FDA-approved treatment for polyneuropathy [Internet]. Pharmaceutical Technology. 2018 [cited 2018Aug22]. Available from: https://www.pharmaceutical-technology.com/news/alnylam-fda-approval-onpattro/.
5. Onpattro[package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.; 2018.
6. Now Approved | ONPATTRO™ (patisiran) [Internet]. ONPATTRO. [cited 2018Aug22]. Available from: https://www.onpattro.com/.
7. Herper M. Alnylam Prices First Gene Silencing Drug At $450,000 Per Patient, But Offers Money-Back Guarantee [Internet]. Forbes. Forbes Magazine; 2018 [cited 2018Aug22]. Available from: https://www.forbes.com/sites/matthewherper/2018/08/10/alnylam-prices-breakthrough-drug-at-450000-per-patient-but-offers-money-back-guarantee/#53c1a0459414.

Special thanks to our peer reviewers:

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DC-CCP Upcoming Events

Announcements for upcoming events to come

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About DC-CCP

DC-CCP is a non-profit professional association and an independent chapter of the American College of Clinical Pharmacy dedicated to improvements in pharmacotherapy practice, education, and research in the Washington D.C. Capital Region, including the District of Columbia, State of Maryland, and Commonwealth of Virginia. Membership will be open to any licensed or registered health care professional or health care professional student in the Capital Region. Membership in the American College of Clinical Pharmacy is not required to become a member of our organization.

Purpose and Goals of DC-CCP

(A) To promote the rational use of drugs in society

(B) To advance the principles and practice of clinical pharmacy

(C) To promote the full-time, advanced practice of clinical pharmacy

(D) To provide an advanced level of continuing education programs in the area of clinical pharmacy and objectives of ACCP as outlined in its constitution and bylaws

(E) To provide a forum for the expression of opinion on pharmacy practice, education, and research from the perspective of clinical pharmacists

(F)To support, promote, and advance the goals and objectives of ACCP as outlined in its constitution and bylaws

(G) To provide a local recruiting base for ACCP

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