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Winter Business Meeting February 4, 2016

## President's Letter

*Dear Colleagues,*

*I hope you are enjoying the sunny days of summer with your family and friends!*

*DC-CCP is excited to have kicked off the season with a great CE session on Hepatitis C. From inpatient, specialty, and to outpatient pharmacy, our variety of speakers certainly generated a lot of great discussion and new clinical practice information for our attending pharmacists and students. Moving forward, we anticipate another successful CE session this fall with pharmacy topics which include oncology, cardiology, and currently "what's new" in pharmacy management trends.*

*In addition, DC-CCP will be engaging our ACCP student chapter affiliations with our upcoming mentorship program and sponsoring and participating with their respective events as another new school year begins soon.*

*Stay cool!  
Best Regards,  
P. Tim Rocafort, PharmD, BCACP  
President, DC-CCP*

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

## Elbasvir/grazoprevir (Zepatier™) [Merck]

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**Drug Class:** NS5A inhibitor/NS3/4A protease inhibitor, fixed-dose combination oral agent

**Indication:** Treatment of chronic (long-lasting) hepatitis C virus (HCV) genotypes 1 or 4 in adults

**Dose:** Elbasvir 50 mg/grazoprevir 100 mg (one tablet) by mouth once daily

**Common adverse effects:** Headache, nausea, trouble sleeping, diarrhea, feeling tired

**Severe adverse effects:** Increases in liver function tests (LFTs)

**Major drug interactions:** Co-administration of moderate CYP3A inducers and strong CYP3A inhibitors (not recommended)

**Resistance Testing:** Testing patients with HCV genotype 1a infection for the presence of virus with NS5A resistance-associated polymorphisms is recommended prior to initiation of treatment with Zepatier™ to determine dosage regimen and duration

The hepatitis C virus (HCV) affects over 170 million people worldwide and is a major cause of cirrhosis and hepatocellular carcinoma.<sup>1</sup> Currently, about 3 million Americans are infected with HCV and the incidence of new cases is rising.<sup>2,3</sup> Since 2007, HCV related deaths in the U.S. have risen to exceed deaths from human immunodeficiency virus (HIV).<sup>1</sup> Unlike the hepatitis A and hepatitis B virus, there is no vaccine available for the prevention of hepatitis C; therefore, the best form of prevention is avoiding behaviors, such as intravenous drug use, known to spread disease.<sup>4</sup>

The HCV infection is treated with antiviral medications to clear the virus from the body, slow progression of inflammation, and reduce the risk of complications like cirrhosis and liver cancer.<sup>5</sup> Until a few years ago, treatment began with 48 weeks of injectable PEGylated interferon and ribavirin (RBV).<sup>1</sup> Due to the route of administration and adverse effect profile of interferon, patients were not able to tolerate this treatment course, which resulted in treatment success to be around 50%.<sup>6</sup> HCV treatment started to advance with the addition of oral direct-acting antiviral (DAA) agents in 2011. These agents, including boceprevir and telaprevir, improved treatment success but still required the use of interferon.<sup>1</sup> In 2013, the FDA approved the first once-daily protease inhibitor, simeprevir, which started the introduction of interferon-free regimens.<sup>5</sup>

In late January 2016, the FDA approved use of Zepatier™ for the treatment of HCV genotypes 1 and 4 in adults.<sup>2</sup> Zepatier™ is an oral, once-daily combination medication of 50 mg elbasvir/100 mg grazoprevir.<sup>6</sup> The following three studies lead to its approval: C-WORTHY, a phase 2 clinical trial, C-EDGE CO-INFECTION, and C-SURFER, both of which are phase 3 studies. The primary endpoint in these studies was SVR12 rates, or the sustained virologic response 12 weeks after the completion of therapy. SVR is defined as an absence of detectable HCV RNA in the serum with use of an assay with a sensitivity of at least 50 IU/mL 6 months after therapy is complete. Table 1 summarizes the differences of each study in terms of patient population, interventions, durations or treatment and results. Each study provides a treatment option for a specific set of patient population with Hepatitis C.

**Table 1.** Comparative studies assessing grazoprevir and/or elbasvir in terms of the patient population, intervention, duration, and results of the study

	<b>C-WORTHY (Lawitz et .al)</b>	<b>C-WORTHY (Sulkowski et. al)</b>	<b>C-EDGE CO-INFECTION (Rockstroh et al)</b>	<b>C-SURFER (Roth et al)</b>
Patient population studied	HCV genotype 1 infection in previously untreated patients with cirrhosis and patients with previous null response with or without cirrhosis.	HCV genotype 1 infection in previously untreated patients without cirrhosis who are HCV mono-infected or HIV/HCV co-infected.	Treatment-naive patients with HCV genotype 1, 4, and 6, with or without cirrhosis, and HIV co-infection (naive to ART with CD4 >500 cells/mm <sup>3</sup> and HIV RNA <50,000 copies/ml or on stable ART for >=8 weeks and with CD4 >200 cells/mm <sup>3</sup> and undetectable HIV RNA)	HCV genotype 1 infection in patients with stage 4-5 CKD
Intervention	Grazoprevir plus elbasvir with or without RBV for 12 or 18 weeks.	8 weeks vs 12 weeks of treatment with grazoprevir and two doses of elbasvir with or without RBV	Grazoprevir and elbasvir fixed-dose combination for 12 weeks. (Single-arm, uncontrolled, non-randomized trial)	Grazoprevir and elbasvir once daily for 12 weeks.
Results (listed as % achieving SVR12)	<p>Previously Untreated with cirrhosis</p> <ul style="list-style-type: none"> <li>• 12wks + RBV - 90%</li> <li>• 12wks without RBV - 97%</li> <li>• 18wks + RBV - 97%</li> <li>• 18wks without RBV - 94%</li> </ul> <p>PR-null response with or without cirrhosis</p> <ul style="list-style-type: none"> <li>• 12wks + RBV - 94%</li> <li>• 12wks without RBV - 91%</li> <li>• 18wks + RBV - 100%</li> <li>• 18wks without RBV - 97%</li> </ul>	<p>HCV Mono-infection</p> <ul style="list-style-type: none"> <li>• 12wks + RBV - 93%</li> <li>• 12wks without RBV - 98%</li> <li>• 8wks + RBV - 80%</li> <li>• 8wks without RBV - not studied</li> </ul> <p>HCV/HIV Co-infection</p> <ul style="list-style-type: none"> <li>• 12wks + RBV - 97%</li> <li>• 12wks without RBV - 87%</li> </ul> <p>*Results using 20mg elbasvir were not individually listed</p>	HIV/HCV Co-infection – 96%	HCV with CKD stage 4-5 – 99%
				Adverse effects occurred at similar frequencies in patient receiving active and placebo drugs.

The C-WORTHY study by Lawitz et al., compared the following: treatment durations of 12 weeks versus 18 weeks, the addition of ribavirin versus no additional ribavirin, and patients with cirrhosis versus patients who were non-responsive with previous PEGinterferon/RBV, defined as PR-null responders, with or without cirrhosis. Treatment duration was randomized between two cohorts: one cohort consisting of previously untreated patients with well compensated cirrhosis (Child-Pugh A) with HCV genotype 1 infection and the second cohort consisting of previously treated patients who were null responders to previous peginterferon plus ribavirin therapy with or without well compensated cirrhosis (Child-Pugh A) with HCV genotype 1 infection. High SVR12 rates were achieved irrespective of population with results ranging from 90% (95% CI 74-98, 28/31; previously untreated with cirrhosis, 12 weeks, with RBV) to 100% (95% CI 89-100; 33/33; PR-null responders, 18 weeks, with RBV).<sup>2</sup> Among the patients who did not receive RBV, 91% (76-98, 30/33) to 97% (95% CI 82-100, 28/29) achieved SVR12. Results from the C-WORTHY study prompted continuation of phase 3 studies for 12 week, non-RBV containing therapy.<sup>6</sup>

An additional C-WORTHY study by Sulkowski et al., compared treatment durations of 12 weeks versus 8 weeks of treatment with grazoprevir and two doses of elbasvir (20 mg or 50 mg) with or without RBV. The patients studied were previously untreated genotype 1 without cirrhosis who were HCV-mono-infected or HIV/HCV co-infected. Results from this study supported that once-daily grazoprevir plus elbasvir with or without RBV for 12 weeks in this specific patient population achieved SVR12 rates of 87-98%, which support the ongoing phase 3 development of grazoprevir plus elbasvir.<sup>7</sup>

HCV infection is a leading cause of morbidity and mortality in patients with HIV. The C-EDGE CO-INFECTION study took the

preliminary results from the C-WORTHY study by Sulkowski, and assessed further the efficacy, safety, and tolerability of Zepatier™ in patients with HCV and HIV co-infection.<sup>8</sup> SVR12 was achieved by 210 of 218 patients (96%; 95% CI 92.9-98.4). Furthermore, all patients with cirrhosis (n=35) achieved SVR12.<sup>8</sup> phase 3 development of grazoprevir plus elbasvir.<sup>7</sup>

HCV infection is a leading cause of morbidity and mortality in patients with HIV. The C-EDGE CO-INFECTION study took the preliminary results from the C-WORTHY study by Sulkowski, and assessed further the efficacy, safety, and tolerability of Zepatier™ in patients with HCV and HIV co-infection.<sup>8</sup> SVR12 was achieved by 210 of 218 patients (96%; 95% CI 92.9-98.4). Furthermore, all patients with cirrhosis (n=35) achieved SVR12.<sup>8</sup>

The C-SURFER study assessed Zepatier™ in patients with stage 4 or 5 chronic kidney disease (CKD). Patients with HCV and CKD have an increased risk of death, yet this patient population has limited treatment options. SVR12 was found to be 99% in the C-SURFER trial (95% CI 95.3-100; 115/116).<sup>9</sup>

Common adverse effects observed in these studies were headache, nausea, fatigue, and diarrhea. Warnings and precautions for Zepatier™ consist of alanine aminotransferase (ALT) elevations and risks associated with RBV containing treatment.<sup>10</sup> Further analysis of side effects will be needed following the extended use of Zepatier™ in the general population. In addition, testing patients with HCV genotype 1a infection for the presence of virus with NS5A resistance-associated polymorphisms is recommended prior to initiation of treatment dosage regimen and duration. Asanta-Appiah et al., found that in subjects receiving Zepatier™ for 12 weeks, SVR12 rates were lower in genotype 1a-infected patients with one or more baseline NS5A resistance-associated polymorphisms at amino acid positions 28, 30, 31, or 93.<sup>12</sup>

In our opinion, Zepatier™ is an effective treatment for the HCV1 and HCV4 virus. Zepatier™ showed safety and efficacy in two difficult to treat patient populations including, patients with stage 4 or 5 CKD and patients with liver cirrhosis. Alternative HCV medications for treatment in this patient population, specifically with these genotypes and comorbidities are on the market; however, at \$54,600 for 12 weeks of treatment, Zepatier™ offers a more cost effective option than these alternatives. Therapeutic pros and cons of each of the possible HCV medications should be considered, in addition to cost, before choosing the optimal HCV treatment. This comparison goes beyond the scope of this introduction to Zepatier™ and would be an ideal topic for further discussions. We believe the role of Zepatier™ in HCV is yet to be clearly defined, but this new agent provides a more reasonably priced alternative to treatment as an oral, once-daily, one tablet formulation.

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## HIV Drug Update: Tenofovir Alafenamide (TAF)

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The nucleotide reverse transcriptase inhibitor (NRTI) tenofovir disoproxil fumarate (TDF) is known to be an effective drug to combat both human immunodeficiency virus (HIV) and hepatitis B virus (HBV). It is considered a mainstay of many HIV regimens and one of the few drugs that can be used to treat both the HBV and HIV effectively.<sup>1</sup> Like most drugs, TDF is associated with side effects which include lowering of bone mineral density, nephrotoxicity and a condition known as Fanconi's syndrome.

To improve the safety profile of tenofovir, a new salt form was developed known as tenofovir alafenamide (TAF), which shows a similar efficacy to TDF but has a safer adverse effect profile. The improved safety profile is due to its stability in plasma, with subsequent intracellular activation by cathepsin A. This results in lower plasma levels of tenofovir diphosphate, while maintaining higher intracellular levels of active tenofovir diphosphate.<sup>2</sup> Due to this activation, TAF can be dosed at up to 1/30 of the dose of TDF.<sup>2</sup>

TAF has been combined with other antiretroviral therapy (ART) agents into a single-tablet regimen (STR). This means that patients with renal or bone density issues are able to get the benefit of a tenofovir-based therapy without the undesired side effects of TDF. A recent study comparing the single-tablet regimen of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide vs. elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate found that patients on both therapies experienced virological suppression at the end of 48 weeks of therapy. Treatment-experienced patients switching to TAF from TDF had significant improvements in urinary biomarkers and improvements in bone mineral density after 48 weeks, similar results were found in renally impaired patients. Overall, therapy.<sup>4</sup>

patients on TAF-based regimens experienced fewer bone and renal toxicities.<sup>2</sup>

The Food and Drug Administration (FDA) recently approved three new ART agents containing TAF: Genvoya<sup>®</sup> (November 5, 2015), Odefsey<sup>®</sup> (March 1, 2016), Descovy<sup>®</sup> (April 4, 2016).<sup>3</sup>

### Genvoya<sup>®</sup>

The first of the tenofovir alafenamide-containing drugs to be approved. The fixed-dose tablet contains elvitegravir, cobicistat, emtricitabine and tenofovir alafenamide 150mg/150mg/200mg/10mg. Genvoya<sup>®</sup> is FDA approved as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older who have no antiretroviral treatment history.<sup>4</sup> Genvoya<sup>®</sup> may replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of Genvoya<sup>®</sup>.<sup>4</sup>

Genvoya<sup>®</sup> is not recommended in patients with a creatinine clearance below 30 mL/min, or in patients with severe hepatic impairment (Child-Pugh Class C). Genvoya<sup>®</sup> is FDA pregnancy category B but there is no human data to support its safety and efficacy in pregnancy; therefore, its use in pregnant women should be based on a risk vs. benefit determination. The use of Genvoya<sup>®</sup> is contraindicated with substrates, potent inhibitors and inducers CYP3A, such as alfuzosin, rifampin, simvastatin, and lovastatin.<sup>4</sup> Genvoya<sup>®</sup> is not approved for the treatment of chronic HBV infection, and its safety in HIV/HBV co-infected patients is yet to be determined. Chronic HBV infection should be ruled out prior to initiation of therapy.<sup>4</sup>

**Odefsey®**

The second of the tenofovir alafenamide-containing drugs that is approved as a complete regimen for treatment-naïve HIV-1 patients who have less than or equal to 100,000 copies per mL of HIV-1 RNA. The fixed-dose tablet is composed of 200 mg of emtricitabine, 25 mg of rilpivirine and 25 mg of tenofovir alafenamide. It is approved for patients 12 years of age and older that are treatment-naïve or are switching to this regimen from another regimen that maintained virological suppression.<sup>5</sup> In addition to screening for renal insufficiency, a patient must be screened for the Hepatitis B virus, as Odefsey® is not approved for Hepatitis B treatment.

When co-administered with drugs that affect CYP3A4 or the P-gp efflux mechanism, Odefsey® has some significant drug-drug interactions. In addition, drugs that increase gastric pH can decrease rilpivirine concentrations; therefore, Odefsey® should be taken 2 hours before or 4 hours after the use of antacids, 12 hours before or 4 hours after the use of H-2 antagonists, and avoided with the use of proton pump inhibitors.<sup>5</sup>

Drugs that can impair renal function should be used with caution due to TAF being renally excreted.<sup>5</sup> Like other TAF-containing drugs, there is no data supporting its use in pregnancy, lactation, pediatrics less than 12 years of age or in patients with severe hepatic impairment.

**Descovy®**

The most recent approval of the tenofovir alafenamide-containing drugs. Descovy® is a two-drug combination of emtricitabine and tenofovir alafenamide, and is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older.<sup>6</sup> Unlike its TDF-containing counterpart

Truvada®, Descovy® is not FDA-approved for use as pre-exposure prophylaxis or for the treatment of chronic hepatitis B virus infection; therefore, HBV infection should be ruled out prior to initiation. Both Truvada® and Descovy® are not recommended for use in patients with a creatinine clearance below 30 mL/min in HIV-1 infected patients. Prior to initiation of Descovy®, creatinine clearance, urine glucose and protein should be obtained for each patient, with continued monitoring during therapy.<sup>6</sup>

**Place In Therapy**

With the exception of Odefsey® (see table), TAF-containing drugs can be used in treatment-naïve patients, regardless of a patient's pretreatment HIV RNA. The newer agents can also be used in treatment-naïve patients with comorbid conditions such as osteoporosis and chronic kidney disease (defined as CrCl below 60 mL/min). For patients who prefer a once-daily tablet, Genvoya® or Odefsey® would be one to consider.<sup>1</sup> It is important to also note that TAF-containing drugs are not recommended in patients with a CrCl below 30 mL/min, also there is no safety or efficacy data in pregnant patients, pediatrics, for their use in PrEP, and in patients with severe hepatic impairment (Child-Pugh Class C).<sup>4,5,6</sup>

Studies have also shown that in treatment-experienced patients with renal impairment (CrCl below 50 mL/min, but above or equal to 30 mL/min) and decreased bone mineral density, switching to a TAF-containing drug actually improved their conditions.<sup>2</sup> Because the TAF-containing drugs have shown similar efficacy and a better safety profile, compared to their TDF-containing counterparts, the newer agents are good alternatives in patients who are candidates for TAF, but are unable to take TDF-containing regimens due to side effects or comorbidities.

**Product Comparison: Tenofovir Alafenamide vs Tenofovir Disoproxil Fumarate<sup>3,4,5,6</sup>**

Drug	Dose	Caveats	Price (monthly)
Genvoya <sup>®</sup>	elvitegravir/cobicistat/emtricitabine/ <b>tenofovir alafenamide</b> 150mg/150mg/200mg/10mg	Not recommended if CrCl is below 30 mL/min	\$3093.19
Stribild <sup>®</sup>	elvitegravir/cobicistat/emtricitabine/ <b>tenofovir disoproxil fumarate</b> 150mg/150mg/200mg/300mg	Do not initiate if CrCl is below 70 mL/min, and discontinue if CrCl is below 50 mL/min	\$3244.76
Odefsey <sup>®</sup>	emtricitabine/rilpivirine/ <b>tenofovir alafenamide</b> 200mg/25mg/25mg	Not recommended if CrCl is below 30 mL/min  Initiate only if pretreatment HIV RNA copies are less than or equal to 100,000 copies/mL	\$2815.04
Complera <sup>®</sup>	emtricitabine/rilpivirine/ <b>tenofovir disoproxil fumarate</b> 200mg/25mg/300mg	Discontinue if CrCl below 50 mL/min  Initiate only if pretreatment HIV RNA copies are less than or equal to 100,000 copies/mL	\$2815.04
Descovy <sup>®</sup>	emtricitabine/ <b>tenofovir alafenamide</b> 200mg/25mg	Not recommended if CrCl is below 30 mL/min	\$1759.59
Truvada <sup>®</sup>	emtricitabine/ <b>tenofovir disoproxil fumarate</b> 200mg/300mg	Discontinue if CrCl is below 30 mL/min in HIV-1 infected patients	\$1759.73

**Key to acronyms:** CrCl= creatinine clearance

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## Role of Mirabegron in Patients Dissatisfied with Initial Antimuscarinic Therapy for Treatment of Overactive Bladder

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Mirabegron (Myrbetriq®) is currently the only  $\beta$ -3 adrenoceptor agonist approved in the U.S. for overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.<sup>1</sup>

Antimuscarinic agents have been the mainstay of OAB therapy; however, due to their mechanism of action, they pose a high risk for adverse effects such as altered mental status, dry mouth, constipation and blurred vision.<sup>2</sup> Mirabegron works as an agonist of human  $\beta$ -3 adrenergic receptors which increases bladder capacity by relaxing the detrusor smooth muscle when the bladder is storing urine during the urinary bladder fill-void cycle.<sup>1</sup>

Mirabegron is currently available in the U.S. as a 25 mg and 50 mg tablet, with a recommended starting dose of 25 mg once daily with or without food and can be titrated to 50 mg once daily based on patient efficacy and tolerability.<sup>1</sup> In patients with severe renal impairment (CrCl 15-29 mL/min or eGFR 15-29 mL/min/1.73m<sup>2</sup>) and/or moderate hepatic impairment (Child-Pugh Class B), dosing should not exceed 25 mg and is currently not recommended for use in patients with end stage renal disease or severe hepatic impairment.<sup>1</sup> Mirabegron is a moderate CYP2D6 inhibitor, therefore appropriate monitoring and dose adjustment may be necessary when co-administered with CYP2D6 substrates, such as metoprolol and desipramine.<sup>1</sup> Although mirabegron showed very low intrinsic activity for  $\beta$ -1 and  $\beta$ -2 adrenergic receptors,  $\beta$ -1 receptor stimulation was reported at higher doses of 200 mg.<sup>1</sup> Therefore, mirabegron is not recommended to be used in patients with severe uncontrolled hypertension ( $\geq 180/110$  mm Hg).<sup>1</sup> The most common adverse effects reported in a

year in which only incidence was reported, were hypertension, dry mouth, constipation, and headache; occurring at a similar incidence across all treatment groups except for dry mouth, which was lower with mirabegron 50 mg (2.8%) vs. tolterodine (8.6%),<sup>3</sup>. In regards to adjusted mean changes from baseline to final visit in systolic blood pressure and pulse rate were 0.2 and -0.5 mm Hg and 0.9 and 1.5 beats per minute for mirabegron 50 mg and tolterodine ER 4 mg, respectively, which are clinically nonsignificant.<sup>3</sup>

According to the American Urological Association (AUA), pharmacologic management of OAB is considered second-line treatment and consists of oral antimuscarinics or oral  $\beta$ -3 adrenoceptor agonists.<sup>2</sup> More specifically, in patients experiencing inadequate symptom control, current AUA guidelines recommendations are vague due to limited studies available at time of publication. Recommendations include either increasing the dose of current therapy, or changing to another antimuscarinic agent or to a  $\beta$ -3 adrenoceptor agonist. At this time, AUA guidelines also do not address the potential role of combination therapy of antimuscarinic agents with  $\beta$ -3 adrenoceptor agonists in patients experiencing inadequate response. Since the AUA guideline publication in 2014, two clinical trials, BEYOND and BESIDES, have been published focusing on the role of mirabegron in patients who were dissatisfied with initial antimuscarinic therapy. Study arms included either switching to another antimuscarinic therapy or to a  $\beta$ -3 adrenoceptor agonist (mirabegron) in the BEYOND study; or considering

*continued on page 10*

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combination therapy with solifenacin/mirabegron or antimuscarinic dose modification in the BESIDES study.<sup>4,5</sup>

BEYOND was a randomized, double-blinded, non-inferiority study in patients dissatisfied with their previous antimuscarinic therapy due to lack of efficacy who were randomized to receive either mirabegron 50 mg or solifenacin 5 mg once daily for 12 weeks. The primary efficacy endpoint was change from baseline to end of treatment in mean number of micturations per 24 hours and secondary endpoint included change from baseline in mean number incontinence episodes per 24 hours. Although reduction in mean daily micturations and incontinence was reported in the mirabegron arm (Table 1), the trial was inconclusive and failed to demonstrate non-inferiority of mirabegron 50 mg compared to solifenacin in primary end point of reducing mean number of micturations.<sup>4</sup> However, similar to previous studies, incidence of adverse effects were similar between both groups, with decreased incidence of dry mouth (3.1% vs 5.8%) reported with mirabegron 50 mg vs. solifenacin 5 mg, respectively.<sup>4</sup>

BESIDES was a randomized, double-blinded, 12-week study including patients with overactive bladder remaining incontinent despite daily solifenacin 5 mg therapy. Patients were randomized to receive either once daily combination (solifenacin 5 mg/mirabegron) or solifenacin 5 mg or 10 mg. Patients on combination therapy with mirabegron were initiated on 25 mg daily and increased to 50 mg daily after week 4. Primary endpoint was change in baseline to end of treatment in mean number of incontinence episodes per 24 hours and secondary end point included mean change in number of micturations per 24 hours. Superiority was tested for combination therapy vs. solifenacin 5 mg and non-inferiority was tested for combination vs. solifenacin 10 mg in secondary endpoint of

mean change in number of micturations. In comparison to solifenacin 5 mg therapy, combination therapy was statistically significant with reducing mean daily micturations (-0.45 (95% CI, -0.67 to -0.22);  $p < 0.001$ ) and mean number of incontinence episodes per 24 hours (-0.26 (95% CI, -0.47 to -0.05);  $p = 0.001$ ) at end of therapy. Combination therapy was superior to solifenacin 5 mg in regards to improvements in daily incontinence and micturations and superior to solifenacin 10 mg in regards to improvements in daily micturations. Incidence of dry mouth and constipation were the most common adverse effects reported, with incidence of dry mouth lower with combination therapy (5.9%) and solifenacin 5 mg (5.6%) compared to solifenacin 10 mg (9.5%).<sup>5</sup>

Based on the above studies, there may be a potential role for mirabegron in combination with an antimuscarinic agent in patients experiencing inadequate symptom control on antimuscarinic monotherapy. Additionally, combination therapy with mirabegron and solifenacin was well tolerated and had lower incidence of dry mouth, compared to dose modification of solifenacin 10 mg. Some limitations of the studies are that both studies were sponsored and analyzed by the drug manufacturer of mirabegron, Astellas, and there was no report on the role of behavioral therapy in conjunction to pharmacologic therapy for overactive bladder, in which is considered first line therapy. Other limitations for mirabegron's use in clinical settings may be due to cost and insurance provisions for use. For a 30 day supply of both mirabegron 25 mg and 50 mg, estimated cost ranged from \$347-\$371. Although most insurance companies cover mirabegron with varying co-pays, some plans may require a prior authorization prior to dispensing.

Table 1:<sup>4,5</sup>

Study Title	N	Duration of Therapy	Mean Change in Number of Micturations per 24 hours at End of Therapy		Mean Change in Number of Incontinence Episodes per 24 hours at End of Therapy	
BEYOND	1887	12 weeks	Mirabegron 50 mg	- 2.95	Mirabegron 50 mg	- 1.40
			Solifenacin 5 mg	- 3.13	Solifenacin 5 mg	- 1.60
BESIDES	2174	12 weeks	<b>Combination*†:</b> <b>(Solifenacin 5 mg + Mirabegron 50 mg)</b>	<b>-1.59</b>	<b>Combination*:</b> <b>(Solifenacin 5 mg + Mirabegron 50 mg)</b>	<b>-1.80</b>
			Solifenacin 5 mg	-1.14	Solifenacin 5 mg	-1.53
			Solifenacin 10 mg	-1.12	Solifenacin 5 mg	-1.67
					Solifenacin 10 mg	

\* Statistically significant difference found compared to solifenacin 5 mg  
 † Statistically significant difference found compared to solifenacin 10 mg

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## Student Pharmacists Celebrate Donate Life Month

Grace Wo, First-Year Student Pharmacist, University of Maryland School of Pharmacy

*\*This event report first appeared on The University of Maryland School of Pharmacy's Blog and has been re-printed with permission*

*Activities held for faculty, staff, and students throughout the month of April raise awareness about the importance of organ donation.*

As student pharmacists at the School of Pharmacy, we are always finding new ways to get involved in improving patient care and raising awareness about important public health topics. Throughout Donate Life Month in April, a group of us collaborated with the Living Legacy Foundation of Maryland to raise awareness about the importance of organ donation to members of the school and local community.

To kick off the month, we held a lightning round question competition on Facebook, where every day we posted a question about organ donation and other students accrued points by answering the question quickly and correctly. Reaching more than 500 people, this event conveyed the impact of organ donation. First-year student pharmacist Leena Doolabh won the competition, and even she was surprised at the new knowledge that she gained from participating, as she remarked, "I couldn't believe that one individual can give life to up to eight other people!"

We also reached out to very diverse populations through tabling events in Pharmacy Hall, at the SMC Campus Center, the Spring Festival in West Baltimore, and various locations on campus. In addition to answering a question about organ donation for a prize, current donors shared why they chose to be organ donors, while others signed up to become donors if they felt ready to commit to that decision. From these events, it became apparent that many people are

impacted by organ donation and transplantation. One woman at the Spring Festival shared a heartbreaking story of her daughter's best friend who passed away after her body rejected her transplanted kidney. Teny Joseph, a first-year student pharmacist and coordinator of the Spring Festival, summarized our group's feelings best when he said, "It was the unexpected moments like these that made our efforts with Donate Life Month worthwhile."

The American Pharmacist Association-Academy of Student Pharmacists (APhA-ASP) general body meeting marked the midpoint of Donate Life Month. In an activity held during the meeting, members were handed a picture of an organ or tissue to represent the organ or tissue they "received." Through this exercise, we were able to help others understand that of the 120,000 people on the waiting list<sup>1</sup>, each person is somebody's mom, dad, child, or friend, and that one donor can save up to eight lives<sup>2</sup>. Following a video about the process of organ donation, Idris Yakubu, PharmD, and Jacqueline Clark, PharmD, transplant pharmacy residents at the University of Maryland Medical Center (UMMC), joined the meeting to answer students' questions about organ donation.

As part of another ongoing event, a story booth was displayed in the Ellen H. Yankellow Grand Atrium in Pharmacy Hall. The "Superhero Story Station" celebrated the stories of Morris Murray and Morgan Yoney. Murray, who was previously diagnosed with HIV, recently received a liver transplant. Diagnosed with cystic fibrosis at a young age, Yoney is still waiting for a match for a lung transplant. Her story can be found on Facebook under *Morgan's Army*. Another member of the first year class, Paul Algire, mentioned how precious it was to him to have an opportunity to participate in Donate Life Month. "My partner's liver transplant three years ago was the catalyst for me to pursue a Doctor of Pharmacy (PharmD) degree. It was great to see so many reminders of that this month," he said.

Later that month, on April 27, a stormy Wednesday was transformed into a Hawaiian paradise in Pharmacy Hall. Students showed up in their most festive Hawaiian shirts to honor Matt Gabriel, a close friend of Ashley Fan, a third-year student pharmacist and coordinator of the event. Hawaiian Shirt Wednesday was a goofy tradition that Matt started during his time at Goucher College. He was heavily involved in the Goucher College community and also a member of the men's lacrosse team.

Unfortunately, on his way home one night, he was hit by a drunk driver and rushed to UMMC. Despite the medical team's best efforts, Matt passed away on April 14, 2014. A liaison from the Living Legacy Foundation of Maryland asked Matt's family if they were willing to honor his wishes to be an organ donor. They agreed, and because of their generosity, his organs saved the lives of four people. Hawaiian Shirt Wednesday raised more than \$300 for the Living Legacy Foundation.

All of these events were made possible by the dedicated work of students tirelessly advocating for a noble cause. Every step of the journey was motivated by the both heartwarming and heartbreaking stories from donors, recipients, and their friends and families. With generous support from the Living Legacy Foundation of Maryland, we reached more than 700 people through in-person events and social media, met 83 existing donors, and helped 11 new individuals sign up to become donors. But regardless of the numbers, we hope that our impact continues far beyond the quantifiable to help others understand the value of becoming an organ donor.

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- 2) Organ Donation Facts. *Live On NY*. 2016. <<http://www.liveonny.org/about-donation/quick-facts-about-donation/>>. Accessed April, 2016

### Special thanks to Communications Committee members and peer reviewers:

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

Please contact [addis228@gmail.com](mailto:addis228@gmail.com)





# DC-CCP Events

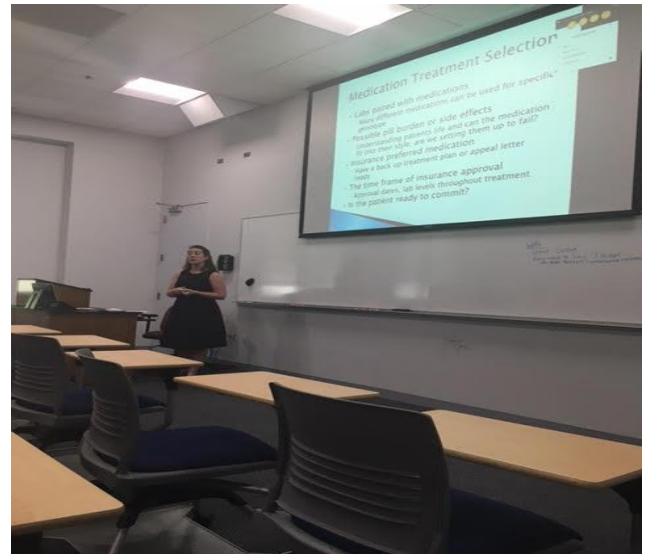


DC-CCP's third annual Advocacy Day on Capitol Hill April 5, 2016



Why Residency? Event held at the Univeristy of Maryland School of Pharmacy- Baltimore April 11, 2016

## DC-CCP Events



DC-CCP Summer CE Event on Hepatitis C Management held at the Universities of Shady Grove June 25, 2016

Photos taken by:

Kevin Nguyen,  
Communications Committee, Student Co-chair

P. Tim Rocafort, Pharm.D, BCACP  
President, DC-CCP

## Upcoming Events

### 2016 ACCP Annual Meeting

October 23-26, 2016  
Hollywood, Florida

### DC-CCP Fall CE Forum

October 29, 2016 9 am-2pm  
Notre Dame University of Maryland  
Baltimore, MD



## 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 therapeutics
- 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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