



ASBMT Pharmacy Special Interest Group (SIG) Newsletter

Letter from the Chair

LeAnne Kennedy PharmD, BCOP, CPP, FHOPA
Chair, ASBMT Pharmacy Special Interest Group

As I have been working this year, I have had many people ask me how do I do all that I do? How to do you maintain your enthusiasm for practice? With over 20 years of practice, this is a common question from new and slightly more seasoned practitioners. They want to know how to prevent burnout. Unfortunately, I don't have a magical answer. I am happy to say that burnout is getting more attention in the literature and press. With a recent survey about burnout from ASBMT and NMDP, pharmacists had the highest percentage of burnout when compared to other HCT practitioners. The advocacy and policy committee is going to be working with other ASBMT committees to address the causes of burnout and try to determine potential solutions for burnout. In the meantime, let me offer a few pearls. What my residents and co-workers often refer to as "Lessons in Life with LeAnne".

Breathe. When you get flustered or frustrated, then take 5-10 seconds and breathe!

Use your resources around you. You don't have to do it all yourself.

Relax. Spend a few minutes a day relaxing/mediating which can help to take the tension away.

Notice the positive things around you! By focusing on the positive, then it helps to prevent the negative thoughts from lingering.

Our patients are our priority. Remember that caring for transplant patients is an honor and that we are here to serve. If you can remember that then it helps to get through those crazy days.

Understand your limits! We can't do it all and as pharmacists we tend to be overachievers but if you remember your limits then you won't overextend yourself.

Take time for yourself!! Find what helps to make you happy and make time for this whether it is running, reading, or resting!

It's been my honor to serve as the chair of the pharmacy SIG this year and look forward to seeing what our SIG and the many hard working pharmacists will do next year.

Inside this Issue:

Letter from the Chair	1
Working Committee Updates	2
ASH Updates	5
Letemovir Prophylaxis in HCT Patients	9
Pharmacy Resident/ Student Q&A	12
New Investigator Award Spotlight	14
Pharmacy SIG Member Highlights	15

Stay up to date with the ASBMT Pharmacy SIG

Please visit us at <http://www.asbmt.org/?PharmacySIG>

ASBMT Pharmacy SIG Working Committee (WC) Updates

Advocacy and Policy Working Committee

In the world of advocacy, winter has shown us no signs of slowing down following a hectic few months. The Advocacy and Policy working committee has been working throughout this busy holiday season on a few special initiatives.

We are currently in the process of creating a task force to assist in a new and very necessary tool in the advocacy and policy world. As new drugs with a role in transplant are approved and come to market, advocates working on behalf of both providers and patients everywhere will work behind the scenes to assist in the delivery of these medications both physically and financially to patients in need. As the experts in medication use throughout the transplant process, a call has gone out via the ASBMT list serve for pharmacists interested in participating on this unique and necessary project. We are currently compiling a list of all pharmacists that have asserted interest and look forward to putting things together in the new year.

As we reflect on this past term, there are many instances of transplant accessibility moving forward on a policy level that should not go unnoticed. Specifically, ASBMT has worked alongside NMDP to bring forward HR 4215 or the Protect Access to Cellular Transplant (PACT) Act. Recently introduced by representatives Erik Paulsen (MN-03), Doris Matsui (CA-06), Gus Bilirakis (FL-12), and Ron Kind (WI-03), this bill would help to line up reimbursement for cord blood, bone marrow, and peripheral blood transplants by stipulating that Medicare provide hospitals the cost of donor search & cell acquisition. This reimbursement would occur on a reasonable cost basis and separately from the

inpatient reimbursement, which is approximately \$65,000. It would align the aforementioned transplant reimbursement provisions with solid organ transplant, including living kidney donor transplants. Currently hospitals may lose several thousands of dollars per transplant as donor searches and cell acquisition are not appropriately reimbursed which may ultimately lead to a loss of access for patients that depend on Medicare. We are excited to see where it will go as Congress resumes their work in 2018.

Lastly, we are happy to continue offering letters of recognition and appreciation to all ASBMT Pharmacy SIG members for the 2017-2018 term. This is our way of showing gratitude on behalf of ASBMT leadership for the time and effort our dedicated members volunteer throughout the months. These letters go directly to the individual managers of each SIG member letting them know how much we appreciate their efforts.

Research Working Committee

The Research WC has continued to work on the establishment of the ASBMT Pharmacy SIG New Investigators Award and are proud to announce our inaugural winner, Dragos Plesca, PharmD, PhD, BCOP. Dragos will be utilizing the 2 year, \$50,000 grant to investigate "Acquired immunity in multiple myeloma patients undergoing maintenance therapy post autologous stem cell transplantation". He will present a brief summary of his project at the 2018 ASBMT Pharmacy Meeting during the Best Oral Abstract program. Stay tuned for more information on the second NIA application process in 2018. Additionally, we continue to collaborate with physicians at M.D. Anderson and the CIBMTR to survey the current use of antibacterial prophylaxis.

(Continued on Page 4)

Membership in the Pharmacy SIG is open to any ASBMT member! If you or someone you know would like to join, please email us at: membership@asbmt.org.

American Society for Blood and Marrow Transplantation Pharmacy Special Interest Group News

(Continued from Page 3)

A question in the recent Pharmacy SIG survey reported that most clinicians are interested in more information on current antifungal practices. We are actively working on future projects to address this topic!

Education Working Committee

The Education WC is currently finalizing an augmented 9-hour live Fundamentals Course at the Annual HOPA conference in 2018 with the intent to provide an interactive case-based experience. This course will take place on Saturday, March 24th and Sunday, March 25th immediately following the conclusion of the HOPA Conference. Registration is open and is linked to the Annual HOPA Conference registration.

The free webinar, "Introduction to HCT" will be broadcasted prior to the conference and is encouraged to be viewed by participants attending the Fundamentals Course.

In collaboration with the Programming Committee, we will be providing on-line cases based on the content of 2 different presentations at the 2018 BMT Tandem Meetings. These cases will be available approximately 2-3 months after Tandem on the Pharmacy SIG website. We have been working diligently with Syntax and Angie Dahl to provide this pharmacy CE opportunity to those members unable to attend live programming.

The 2017 update to the Standards of Care Guidelines and Resource Links will be available by the end of January 2018. We are also happy to be adding content specifically targeted toward pediatric practice. The 2016 version is currently available on the ASBMT Pharmacy SIG website, (<http://asbmt.org/page/standard-of-care-guidelines-and-resource-links>). The website navigation for this large and detailed body of information has been improved; hopeful-

ly you will find it more user-friendly. Our committee plans to update this collection of key articles biannually.

Program Planning Working Committee

We hope to see you all at the BMT Pharmacists' Conference at the upcoming 2018 ASBMT Tandem Meetings in Salt Lake City, Utah! This year's conference will be held February 23rd and 24th at the Salt Palace Convention Center. Preparations are underway for another year of relevant and timely discussions on topics of interest to pharmacists and providers practicing in the area of BMT. Topics will include the crowd favorites, "ASH Update," "New and Emerging Drugs," and the "Challenging Cases" series, as well as topics of current interest, an expert panel discussion: "Best Practices: An Update on CAR-T Cells and CRS Management" and a novel "Cannabinoid Consult Service" practice in Colorado.

Pharmacists will be presenting at the Tandem Meetings' Poster Sessions, with the top 4 pharmacist-submitted abstracts selected to present podium presentations during the BMT Pharmacists Conference.

At the 2018 Meetings, we will be introducing a speaker mentorship program for new speakers interested in presenting at an upcoming Tandem meeting, and will be sending out a call for mentors willing to help guide these interested speakers.

We are also planning on providing those unable to attend the meeting with the opportunity to obtain 2 BMT Pharmacist CEs through presentations delivered at the meeting, through our new Enduring Education Cases initiative. These Pharmacist CEs will be free to all members and posted on the ASBMT Pharmacy SIG website following the meeting. More details to follow.

(Continued on Page 5)

Important Dates

2018 BMT Pharmacists Conference

February 23-24, 2018
Salt Lake City, UT

BMT Fundamentals Course

March 24-25, 2018
Denver, CO (HOPA Annual Conference)

American Society for Blood and Marrow Transplantation Pharmacy Special Interest Group News

(Continued from Page 4)

For those planning on attending the Tandem meetings, please plan to join us after our first day of programming (Friday the 23rd), from 6-8 PM, for the Pharmacy SIG reception and networking session! It's always a great time to network with other HCT pharmacists and catch up with colleagues! Hope to see you there!

Communications Working Committee

The Communication Working Committee continues to keep the Pharmacy SIG informed of committee activities and ongoing projects through the biannual newsletter. In addition, the WC has focused on recognizing our many accomplished HCT pharmacists through member spotlights and highlights. Check out "Awards and Publications" on pages 15-16 of this Newsletter. The Communications WC maintains its educational endeavors through pharmacy resident contributions and summaries of key events or studies from the American Society of Hematology's Annual Meeting and the Tandem Meetings in our newsletters, as well as monthly summaries of literature affecting HCT practice distributed through the email listserv.

The ASBMT Pharmacy SIG website is consistently updated with "News" and "Events" sections for easy access to the latest and greatest from the Pharmacy SIG. Check out the website at <http://asbmt.org/about-us/special-interest-groups/pharmacy-sig>.

The Communications WC encourages pharmacy students and residents interested in HCT Pharmacy to submit questions to be answered in our student/resident Q&A section of the newsletter. We also welcome all feedback on any of the communication methods above. Please send questions and suggestions to ASBMTPharmacySIG@gmail.com.

Membership and Awards Working Committee

The ASBMT Pharmacy SIG is now 255 members strong and growing! This fall, the Membership and Awards WC has been busy collaborating with the Advocacy and Policy WC in creating a Pharmacy SIG recruitment brochure to use at the Tandem Meetings. Additionally, we collaborated with all WCs to send out the 2017 member survey to learn what you find valuable about SIG membership and how we can support our members in the future. But the most rewarding part of our fall was reviewing the many deserving nominations for our 3 membership awards; Lifetime Achievement, New Practitioner, and Excellence in Advocacy. The elevated level of practice, dedication to our patients/profession and well as the respect from colleagues in all areas of our HCT community is inspiring. We congratulate all of our nominees and thank the nominators for recognizing these talented individuals! We hope all of you will be able to join us in Salt Lake City for the Tandem Meetings where these awards will be presented.



Want to become part of an ASBMT

Pharmacy SIG Working Committee?

We are seeking enthusiastic and motivated HCT pharmacists! Applications for qualified candidates are being taken until February 5, 2018.

For more information, visit:

[http://asbmt.org/about-us/special-interest-groups/
pharmacy-sig](http://asbmt.org/about-us/special-interest-groups/pharmacy-sig)



2017 ASH Update

Elizabeth DiMaggio, PharmD, BCOP

ASH was held December 9-12, 2017 in Atlanta, GA and these are the pertinent, pharmacy-related abstracts from the meeting:

Abstract 401: Double Autologous Stem Cell Transplantation Significantly Prolongs Progression-Free Survival and Overall Survival in Comparison with Single Auto transplantation in Newly Diagnosed Multiple Myeloma: An Analysis of Phase 3 EMN02/HO95 Study

- Phase III study randomizing newly diagnosed (ND) patients with multiple myeloma (MM), median age 58 years, in a 1:1:1 fashion to treatment with bortezomib-melphalan-prednisone (VMP), single autologous hematopoietic transplantation (aHCT), or double aHCT following induction with bortezomib, cyclophosphamide, dexamethasone (VCD)
- The 415 patients receiving aHCT (single [ASCT-1] vs. double [ASCT-2]) were compared with the endpoint of progression free survival (PFS)
- Three-year estimated PFS was 72.5% (95% CI=66.2-79.4) for ASCT-2 group vs 65% (CI=57.3-71.5) for ASCT-1 group (Hazard ratio [HR]=0.71; CI=0.50-0.98; P=0.040)
- Three-year overall survival (OS) was 89% (95% CI=84.4-93.7) for ASCT-2 group vs 81.5% (95% CI=76-87.5) for ASCT-1 group (HR=0.51; CI=0.31-0.86; P=0.011)

Abstract 398: Bortezomib and High-Dose Melphalan vs. High-Dose Melphalan as Conditioning Regimen before Autologous Stem Cell Transplantation in De Novo Multiple Myeloma Patients: A Phase 3 Study of the Inter-groupe Francophone Du Myelome (IFM 2014-02)

- Phase 3, randomized, multicenter, open label trial with ND MM receiving aHCT with either high dose melphalan (HDM, n=154) or melphalan combined with bortezomib (Bor-HDM, n=146)
- Complete response (CR) at day +60 was the primary endpoint of which there was no difference found between the arms: 23.4% in Bor-HDM vs. 20.5% in HDM (p=0.72) in the intent-to-treat (ITT) analysis
- Progression free survival (PFS) and OS were also similar; PFS was 78.5% in the Bor-HDM arm vs. 79.9% in the HDM arm (P=0.4232) while OS was 93.4% in the Bor-HDM arm and 99.3% in the HDM arm (p=0.1277)
- Incidence of grade 3/4 toxicities was slightly higher in the Bor-HDM arm (67% vs 63%)

Abstract 399: A Randomized Phase III Trial of Busulfan + Melphalan Vs Melphalan Alone for Multiple Myeloma

- Randomized phase III trial including 204 MM patients, median age 59, undergoing aHCT with either HDM or busulfan plus melphalan (Bu-Mel) to determine efficacy (PFS, OS, response rates) and safety
- Patients were well balanced with regard to age, gender, stage (international staging system [ISS] and revised ISS), response to induction, and cytogenetic risk
- Diarrhea grade 1-3 was lower in patients receiving Bu-Mel compared with HDM (57% vs. 78%, p=0.002) while grade 1-3 mucositis (96% vs. 49%, respectively, p <0.001), liver abnormalities (increase ALT, 33% vs 1%, respectively, p <0.001), and neutropenic fever (71% vs. 30%, respectively, p <0.001) were all higher

(Continued on Page 7)

2017 ASH Update (cont.)

(Continued from Page 6)

- No difference was found in CR at day +100 between Bu-Mel vs. HDM ($p=0.22$), final CR ($p=0.57$), nonrelapse mortality (NRM) at day +100 ($p=1.00$) or 1 year ($p=0.11$), and OS ($p=0.94$) but median PFS was significantly longer (64.7 mo vs. 34.4 mo, $p=0.013$) in the Bu-Mel arm

Abstract 598: Allogeneic Hematopoietic Cell Transplantation for Acute Myeloid Leukemia and Myelodysplastic Syndrome: Effect of Transplant Conditioning Regimen Intensity on Outcomes

- Large retrospective multicenter study including patients from the Center for International Blood and Marrow Transplant Research (CIBMTR) database with AML \geq CR 1 ($n=1258$) and myelodysplastic syndrome (uni-or multi lineage dysplasia, 5q- syndrome or refractory anemia with excess blasts [RAEB], $n=951$) with the aim of identifying the optimal regimens (busulfan with cyclophosphamide, Bu/Cy; fludarabine with busulfan doses 10-13 mg/kg, Flu/Bu 4; fludarabine with busulfan doses 5-6 mg/kg, Flu/Bu 2; fludarabine with melphalan, Flu/Mel)
- Antithymocyte globulin (ATG) was used most often for in vivo T cell depletion
- Compared to Bu/Cy, NRM, relapse, treatment failure, and OS were not different than Flu/Bu 4, but when ATG was added, Flu/Bu 4 had greater relapse and higher mortality ($P<0.05$). Flu/Mel without ATG had lower relapse rates than Bu/Cy ($P<0.05$)
- When only reduced intensity conditioning (RIC) regimens were compared, Flu/Mel resulted in higher NRM but lower relapse and lower treatment failure than Flu/Bu 2 with and without ATG

Abstract 909: Busulfan Fludarabine (BU-FLU) Compared to Thiotepa Busulfan Fludarabine (TBF) for Allogeneic Transplants in Acute Myeloid Leukemia or Refractory Anemia with Excess Blasts in Remission

- Multicenter study comparing Bu-flu ($n=157$) to TBF ($n=127$) in patients with AML or RAEB in CR1 and CR2, median age of 53 years, undergoing hematopoietic cell transplantation (HCT) from matched related donors (MRD) and matched unrelated donors (MUD), including haploidentical donors
- Grade II-IV and III-IV graft versus host disease (GVHD) was similar in both arms ($p=0.8$ and $p=0.7$, respectively)
- Transplant-related mortality (TRM) was similar at 16% for Bu-Flu vs. 9% for TBF ($P=0.09$) while more patients relapsed receiving Bu-Flu (28% vs. 21%, $p=0.04$)
- Overall survival was significantly improved with TBF at 82% compared with Bu-Flu at 51% ($p=0.0002$)

(Continued on Page 8)

2017 ASH Update (cont.)

(Continued from Page 7)

Abstract 215: Cyclophosphamide (PT-Cy) for Graft Versus Host Disease (GVHD) Prophylaxis in Allogeneic Transplantation from HLA Identical Sibling and Matched Unrelated Donor for Patients with Acute Leukemia, on Behalf of ALWP-EBMT

- Multicenter retrospective study on behalf of the Acute Leukemia Working Party and European Society for Blood and Marrow Transplantation evaluating the use of post-transplant cyclophosphamide (PTCy) GVHD prophylaxis in 423 acute leukemia patients undergoing HCT with either a matched sibling donor (MSD) or MUD
- Prophylaxis included PTCy alone (n=78), PTCy with one additional immunosuppressant (cyclosporine [CsA] or methotrexate [MTX] or mycophenolate mofetil [MMF]), or PTCy with two immunosuppressant agents (CsA + MTX, or CsA + MMF)
- Overall, grade II-IV acute GVHD, chronic GVHD, and extensive chronic GVHD was 27.9%, 33.4%, and 16.5% respectively. Two-year relapse, leukemia free survival (LFS), and OS was 33.5%, 48%, and 55%, respectively

Abstract 665: Severe Cytokine Release Syndrome (CRS) Is a Fatal Complication after PBSC, but Not after BM Haploidentical Transplantation with Post-Transplant Cyclophosphamide

- Retrospective study including 66 patients undergoing a haploidentical HCT (haplo-HCT) receiving PTCy as part or all GVHD prophylaxis with either peripheral blood stem cells (PBSC, n=38) or bone marrow (BM, n=28)
- Patients were similar in age, disease status prior to HCT, Sorror score, conditioning intensity, donor age and type
- Cumulative incidence of grade >1 CRS was 84% (95% CI: 67-93) with the PBSC graft and 64% (95% CI: 43-79) with the BM grafts with a median time from infusion to CRS of 1 (0-7) and 2 (0-4) days, respectively, after Haplo-HCT
- Severe CRS (grade ≥ 3) only occurred with PBSC grafts with a cumulative incidence of 16% (95% CI: 6-29). CRS ≥ 3 compared with CRS <3 resulted in worse 1-yr NRM (75% vs. 15%, p=0.008, respectively) and 1-yr OS (73% vs. 25%, p=0.006, respectively)

Abstract 664: Evaluation of Infectious Complications after Haploidentical Stem Cell Transplantation in Adult Patients with Hematologic Malignancies

- Single center, retrospective analysis evaluating the incidence of infections in 72 consecutive patients regardless of diagnosis, disease status, and conditioning, undergoing haplo-HCT (with either BM or PBSC as the graft source) and PTCy+CsA+MMF for GVHD prophylaxis
- Median time to absolute neutrophil recovery was 17 days (12-88). Overall, the incidence of bacterial infections, fungal infections, and viral infections at day +100 was similar to 2-year post haplo-HCT

(Continued on Page 9)

2017 ASH Update (cont.)

(Continued from Page 8)

Abstract 666: Transplant-Associated Thrombotic Microangiopathy (TA-TMA): Not a Singular Entity

- Single center retrospective cohort analysis to determine the incidence, etiology, treatment and outcomes patients with confirmed TA-TMA (N=215)
- TA-TMA was present in 7% of patients by day +100 in patients receiving first HCT and 12% in patients receiving subsequent HCTs; median onset time was 62 days (35-93). The most common complications that preceded TA-TMA was either refractory GVHD or acute GVHD
- Patients with disease recurrence and systemic infection preceding TA-TMA had the worst overall survival
- Calcineurin inhibitor cessation or switch (32%) was the most common treatment

Abstract 335: Late Fatal Infections (LFI) Remain Higher Than Expected in Adults Receiving Allogeneic Stem Cell Transplant

- Large (N=10,336) multicenter retrospective study from the CIBMTR database evaluating the incidence and type of infection, and associated factors, in allogeneic HCT recipients, median age 44 (18-79) who are surviving disease-free 2 years later
- Overall, 22% of patients (n=2,245) died ≥ 2 years post HCT of which 31% of deaths (n=687) were due to infections
- When infection was the primary cause, not contributing cause, unspecified infections were the most common cause of infectious death (37%) followed by documented bacterial infections (35%). When infections were the contributing cause, bacterial infections (46%) were the most common cause of death, followed by unspecified infections (26%)
- From 3 to 12 years post HCT, the cumulative incidence of infection increased from 2% – 6%
- Increased age, male gender, unrelated HCTs, TBI conditioning, and chronic GVHD on immunosuppression all contributed to late fatal infections

Look forward to our next newsletter which will include pharmacy-related abstracts presented at the ASBMT Tandem Meeting!

Letermovir: A Novel Antiviral for Cytomegalovirus Prevention in Hematopoietic Stem Cell Transplant

Jordan Baskett, PharmD; PGY-2 Oncology Pharmacy Resident
Vanderbilt University Medical Center, Nashville, TN

Cytomegalovirus (CMV) infection is responsible for significant morbidity and mortality in immunocompromised patients undergoing hematopoietic stem cell transplantation (HCT). Prevention of CMV infection with antiviral agents positively impacts patient survival although the common side effects of myelosuppression and renal toxicity limit the use of various antiviral medications. As a result, the majority of transplant programs utilize a pre-emptive therapy approach to initiate treatment at first detection of CMV reactivation rather than using universal prophylaxis. Letermovir (Prevymis™) was recently approved by the US Food and Drug Administration (FDA) for the prophylaxis of CMV infection and disease in adult CMV-seropositive recipients of an allogeneic HCT.¹ Letermovir has a unique mechanism of action against CMV and a favorable side effect profile, particularly in the HCT population.

Developed as a novel compound, letermovir had undergone phase I and IIa clinical trials by 2009.² Compared to reference compound ganciclovir, letermovir exhibited very potent *in vitro* antiviral activity and its inhibitor potency surpassed ganciclovir by more than 2000-fold with respect to the approximate 90% effective concentration.³ In 2010, the medication was compassionately used in a lung transplant patient with multidrug-resistant CMV disease.⁴ This was the first documented use of letermovir in the treatment of CMV disease; the patient had disseminated multidrug-resistant CMV disease and had failed treatment with multiple agents including ganciclovir, foscarnet, cidofovir, and leflunomide. Concurrently on tacrolimus, the patient was initially dosed at letermovir 120 mg daily based on

phase I pharmacokinetic data, but was increased to 240 mg daily due to disease severity and good tolerability. After 28 days of treatment, the CMV viral load was below the limit of quantification after more than 5 months of viremia. By early 2011, the European Commission granted letermovir orphan drug designation for prevention of CMV disease.² The FDA then granted it a fast track designation in August 2011, and the results of a phase IIb trial in bone marrow transplant recipients were presented at various meetings by 2012.⁵

“Letermovir may have a niche in clinical practice but pharmacists will have to decide when to best utilize this medication to improve patient care and outcomes.”

Letermovir is a CMV DNA terminase complex inhibitor with activity against CMV that is resistant to CMV DNA polymerase inhibitors such as ganciclovir, foscarnet, and cidofovir.^{1,2} The CMV DNA terminase complex is a collective group of proteins that enable maturation and termination of long DNA chains into functional monomers and then package the monomers into a viral capsid prior to its release as an infective virion. The DNA terminase complex is vital to CMV replication and inhibiting this complex causes cell destruction. Due to this unique mechanism, letermovir-resistant CMV does not exhibit cross-resistance with currently approved antiviral medications.

(Continued on Page 10)

American Society for Blood and Marrow Transplantation Pharmacy Special Interest Group News

(Continued from Page 9)

Letermovir is available in two formulations, an oral tablet as well as a one hour intravenous infusion. The recommended dosage is 480 mg administered orally or intravenously once daily; a dose reduction to 240 mg once daily is needed if the patient is concomitantly taking cyclosporine. Dosage adjustments are not required for patients with creatinine clearance greater than 10 mL/min, though serum creatinine must be closely monitored in patients with creatinine clearance less than 50 mL/min receiving the injection because the intravenous vehicle, hydroxypropyl betadex, can accumulate. While not recommended for patients with severe hepatic impairment, no dosage adjustment is required for patients with mild or moderate hepatic impairment.

The safety and efficacy of letermovir was evaluated in a multicenter, double-blind, placebo-controlled phase III trial in adult CMV-seropositive recipients of an allogeneic HCT.⁶ Subjects were randomized (2:1) to receive letermovir or placebo starting between day 0 and day 28 post-transplant and continued through week 14 post-transplant. Randomization was stratified by investigational site and risk level for CMV reactivation at the time of study entry. At baseline, 30% of all subjects had at least one factor associated with increased risk for CMV reactivation (high-risk stratum) including Human Leukocyte Antigen (HLA)-related donor with at least one mismatch, haploidentical donor, unrelated donor with at least one mismatch, use of umbilical cord blood as stem cell source, use of *ex vivo* T-cell-depleted graft, and Grade 2 or greater graft-versus-host disease (GVHD) requiring systemic steroids. The remaining 70% of subjects were included in the low-risk stratum.

The primary endpoint was the incidence of clinically significant CMV infection through week 24 post-transplant

(failed prophylaxis).⁶ In the study, 38% of patients who received letermovir (n=325) failed prophylaxis compared to 61% of patients who received placebo (n=170). The treatment difference in percent response calculated using stratum-adjusted Mantel-Haenszel method was -23.5 (-32.5, -14.6; p<0.0001). At week 14, there was a significant difference in the cumulative rate of clinically significant CMV infection with 6.8% for letermovir versus 41.3% for placebo (p<0.0001). Reduction in the risk of clinically significant CMV was observed for letermovir in both the high risk (p<0.0001) and low risk for CMV strata (p<0.0001). The percent of early discontinuations were similar between study arms (17% for letermovir vs 16% in the placebo arm), and discontinuation secondary to adverse events was minimal (1.8% vs 0.6%, respectively). The most common adverse events in each group, respectively, were GVHD (39.1% vs 38.5%), diarrhea (26% vs 24.5%), and nausea (26.5% vs 23.4%). The safety and efficacy data from this trial gained letermovir FDA approval.

Letermovir has several advantages over current antiviral options, though limitations exist as well. In addition to the lack of cross-resistance, the ease of administration as a once daily oral tablet or intravenous injection allows patients to continue their daily activities without being hospitalized. Additionally, the adverse event profile is greatly improved compared to other anti-CMV medications particularly in terms of nephrotoxicity and myelosuppression; nausea and diarrhea were the most commonly reported adverse events in trials. Letermovir appears to be a promising option for CMV prevention in the HCT population, though its use may be limited because of its specificity for CMV.

(Continued on Page 11)

American Society for Blood and Marrow Transplantation Pharmacy Special Interest Group News

(Continued from Page 10)

Immunocompromised patients who have undergone a HCT require prophylaxis against multiple viruses, including herpes-simplex virus, which letermovir does not have activity against. Another limitation may be medication cost; the wholesaler acquisition cost per day is \$195 for the tablets and \$270 for the injection. The Merck Access Program provides co-pay assistance options for eligible patients which can help reduce medication cost for some individuals.

Letermovir may have a niche in clinical practice but pharmacists will have to decide when to best utilize this medication to improve patient care and outcomes. Based on the phase III data, patients undergoing HCT who are deemed high-risk for CMV reactivation are most likely to benefit from letermovir prophylaxis. While patients in the low-risk stratum also had benefit, the cost-effectiveness in this patient population is likely not be as well defined. Patients at risk for renal dysfunction or prolonged myelosuppression would benefit from this antiviral agent as opposed to others available on the market due to the much improved side effect profile and good tolerability. Currently FDA approved only for CMV prevention, letermovir certainly has the potential to be used for CMV treatment as well, especially in patients with multidrug resistant disease. Future studies and more experience with this medication are needed to fully understand its role in CMV prevention and treatment.

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Would you like to write an educational piece for the next Pharmacy SIG Newsletter?

We are always seeking HCT practitioners
or PGY2 oncology residents who are eager
to contribute to the education of our SIG!

Please contact us for more
information or to volunteer:
ASBMTPharmacySIG@gmail.com

Pharmacy Student and Resident Q&A

Question: Do you feel the roles of stem cell transplant pharmacists have changed in recent years or will change in the future?

Answered by:
Shreya Shah, PharmD, BCOP
Sylvester Comprehensive Cancer Center
University of Miami Health System—Miami, FL

Answer:

The role of the stem cell pharmacist is very different depending on the type of institution you are practicing at. There are several institutional factors that shape your role including the volume and complexity of the stem cell transplant service, the number of stem cell pharmacists at the institution, and the age of the program. In programs that are new or have lower volumes, the pharmacist focuses more on the regulatory aspect of care including creating stem cell standard operating procedures (SOPs), educating various types of clinicians and healthcare providers within the institution, and developing clinical care guidelines to offer the highest level of care to obtain and maintain your FACT accreditation. In more established programs there tends to be a much larger clinical, teaching, and research component to the pharmacist's role. An exciting new development in the field of oncology is the introduction of chimeric antigen receptor T-cell (CAR-T) therapy. Many of institutions and pharmacists are gearing up to offer this novel therapy as standard of care. One caveat is that each center is handling CAR-T therapy a little differently, and the role of the stem cell program and pharmacist may differ. Implementing a new service line or program like CAR-T therapy can be somewhat similar to starting a new stem cell program.

There are the parallel processes of creating SOPs, clinical care guidelines to monitor, evaluate, and manage the unique toxicities of CAR-T therapy, building chemotherapy order sets, and developing large-scale educational initiatives involving multiple disciplines (i.e. finance, social workers, pharmacy, nursing, doctors and allied health professionals, and critical care teams). Furthermore, there are a few notable differences between CAR-T therapy and stem cell transplant. CAR-T therapy requires a complex risk evaluation mitigation (REMs) program mandated by the FDA. In addition, there are several other T-cell based immunotherapies targeting a wide array of disease states in the pipeline. If CAR-T therapy or any other novel T-cell based immunotherapies are in the plans for your institution, your role as a stem cell pharmacist may become very challenging yet rewarding over the next few years. Always keep in mind, your traditional role as a stem cell pharmacist will vary based on your center of practice, and more importantly will always experience upcoming transformations given the rapid development of novel therapies in our field. It is and will continue to be an exciting time to be a stem cell pharmacist!

“...your role as a stem cell pharmacist may become very challenging yet rewarding over the next few years.”

Do you know a pharmacy resident or student with questions for a HCT pharmacist?

We would like to answer them! Please email us at: ASBMTPharmacySIG@gmail.com.

Pharmacy Student and Resident Q&A

Question: What recommendations do you have for other transplant pharmacists who want to get involved with research at their institution?

Answered by:
Alex Ganetsky, PharmD, BCOP
Hospital of the University of Pennsylvania —
Philadelphia, PA

Answer:

There are multiple strategies that can be utilized for transplant pharmacists to get involved in research. One approach involves obtaining official training via a certificate program or a graduate degree in programs focused on developing strong, independent researchers, which may include (but certainly not limited to) a focus on Translational Research, Clinical Epidemiology, Biostatistics or Pharmacology. It may be even more beneficial to select a program that requires a thesis, as this creates an opportunity to spearhead a robust research project from scratch. Another mechanism that can be used to become involved in research is to identify a senior researcher at your institution and ask to participate in a study they are directly involved with. Working closely with a senior researcher who possesses strong mentoring skills can often be the best training one can receive. Additional strategies that can be employed include working with faculty at an affiliated College of Pharmacy, volunteering to work with pharmacy residents on their research projects, and volunteering for BMT-focused research committees within various organizations.

**Register for the 2018
*Fundamentals of Hematopoietic
Cell Transplantation (HCT)
Training Course!***

This program is held immediately following the 2018 HOPA Annual Conference in Denver, CO from **March 24-25, 2018**. The course provides 9 hours of CE and focuses on the skills required to care for HCT patients, particularly the pharmacotherapeutic management of patients throughout the transplant process.

For more information, please visit:
<http://www.hoparx.org/annual-conference/preconference-sessions>



ASBMT Pharmacy SIG New Investigator Award Recipient: Dragos Plesca, PharmD, PhD, BCOP

The ASBMT Pharmacy SIG New Investigator Research Award is presented to an individual who is within the first 7 years after his or her post-doctoral training to support research costs in the field of blood and marrow transplantation. Dr. Dragos Plesca is the recipient of this inaugural award, which will fund his research project, "Acquired immunity in multiple myeloma patients undergoing maintenance therapy post autologous stem cell transplantation." He will accept the award at the 2018 ASBMT Tandem Meeting in February.

Plesca completed his Doctor of Pharmacy studies at the University of Medicine and Pharmacy "Carol Davila," in Bucharest, Romania and earned his Doctor of Philosophy degree in cellular and molecular biology, specializing in cancer biology, from Kent State University and Cleveland Clinic. He completed his pharmacy practice and oncology residency training at Cleveland Clinic, Cleveland, OH and then joined the department of pharmacy at Carolinas Medical Center, Charlotte, NC as the clinical pharmacy specialist in adult hematology/oncology and hematopoietic stem cell transplantation. He is board certified in oncology and is currently the Oncology Clinical Pharmacy Manager at the Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC.

Plesca is the immediate past-chair of the ASBMT Pharmacy SIG Research Working Committee and is currently a member of this committee. He is the PGY2 Oncology Pharmacy Residency Program Director and served as the chair of the Residency Research Subcommittee. In these roles he mentors trainees as well as new practitioners in various re-

search studies aimed at improving the outcomes of patients with cancer. Plesca gives the following research advice to new pharmacists: "Any question to which your answer starts with 'I don't know' or 'I'm not sure' can potentially be turned into a great research project. The most important part is not to stop after 'I don't know'."

Plesca has been involved in numerous bench, clinical, and translational research studies in hematologic malignancies. His early research focused on understanding the molecular mechanisms and interplay among DNA repair, cell cycle and apoptosis in hematopoietic cancer cells in response to ionizing radiation. Later on, a major area of his clinical research has been in acute leukemias, lymphomas and multiple myeloma, attempting to improve clinical outcomes in disease treatment or supportive care. He also serves as co-investigator on various studies aimed at improving the outcomes of patients undergoing stem cell transplantation (stem cell mobilization and collection, genotype-guided dosing of antifungals and tacrolimus).

Congratulations to Dr. Dragos Plesca on this outstanding honor and his remarkable commitment to research in the field of blood and marrow transplantation.



Pharmacy SIG Member Highlights

Member Spotlights in 2017:

LeAnne Kennedy, PharmD, BCOP, CPP, FHOPA;

Ali Cook, PharmD; Brandi Anders, PharmD, BCOP, CPP

- American Society of Health-System Pharmacists (ASHP) 2017 Best Practice Award for the Evaluation of a Pharmacist Led Outpatient Autologous Hematopoietic Stem Cell Transplantation Program



Pictured (from left to right): Dianna Howard, Brandi Anders, LeAnne Kennedy, Ali Cook, Brian Marlow

Amber Clemmons, PharmD, BCOP

- 2017 Hematology/Oncology Pharmacy Association (HOPA) New Practitioner Award



Pictured: Amber Clemmons receiving her award

Member Publications in 2017:

- Singh A, **Parmar S**, Patel K, **Shah S**, Shore T, Gergis U, Mayer S, Phillips A, Hsu J-M, Niesvizky R, Mark T, Pearse R, Rossi A, and van Besien K. Granulocyte Colony-Stimulating Factor Use After Autologous Peripheral Blood Stem Cell Transplantation: Comparison of Two Practices. *Biol Blood Marrow Transplant*. 2017. Epub. <https://doi.org/10.1016/j.bbmt.2017.10.026>.
- Clemmons AB**, Gandhi A, Albrecht B, Jacobson S, Pantin J. Impact of Fluoroquinolone Prophylaxis on Infectious Related Outcomes after Hematopoietic Cell Transplantation. *Journal of Oncology Pharmacy Practice*. 2017; DOI: 10.1177/1078155217735153.
- Borg M, **Clemmons AB**. Venetoclax: A Novel Treatment for Patients with del(17p) Chronic Lymphocytic Leukemia. *Journal of the Advanced Practitioner in Oncology*. 2017; Sept/Oct; 8: 647-52.
- Stover JT, **Shaw JR**, Kuchibhatla M, Horwitz ME, **Engemann AM**. Evaluation of Hematopoietic Stem Cell Mobilization Rates with Early Plerixafor Administration for Adult Stem Cell Transplantation. *Biol Blood Marrow Transplant*. 2017;23(8):1290-94.
- Ulrickson ML, Puri A, Lindstrom S, Cassaday RD, **De Padova N**, Becker PS. Gemcitabine and docetaxel as a novel treatment regimen for blastic plasmacytoid dendritic cell neoplasm. *Am J Hematol*. 2017; 92(5):E75-E77. Epub. DOI: 10.1002/ajh.24696.
- Gatwood J, **Gatwood K**, Gabre E, **Alexander M**. Impact of clinical pharmacists in outpatient oncology practices: A review. *Am J Health Syst Pharm*. 2017;74(19):1549-57.
- Neelapu SS, Tummala S, Kebriaei P, Wierda W, Gutierrez C, Locke FL, Komanduri KV, Lin Y, Jain N, Daver N, Westin J, **Gulbis AM**, Loghini ME, de Groot JF, Adkins S, Davis SE, Rezvani K, Hwu P, Shpall EJ. Chimeric antigen receptor T-cell therapy – assessment and management of toxicities. *Nat Rev Clin Oncol*. 2017. Epub. DOI: 10.1038/nrclinonc.2017.148.

(Continued on Page 16)

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Pharmacy SIG Member Highlights

(Continued from Page 15)

- **Hammerstrom AE, Lombardi LR, Pingali SR, Rondon G, Chen J, Milton DR, Chemaly RF, Champlin RE, Gulbis A, Ciruea SO.** Prevention of Cytomegalovirus Reactivation in Haploidentical Stem Cell Transplantation. *Biol Blood Marrow Transplant.* 2017. Epub. DOI: 10.1016/j.bbmt.2017.09.018.
- **Bryk A, Koontz S, Mayor J, Betcher J, Tombleson R, Bookout R, Saunders IM.** Characterization of collaborative practice agreements held by hematopoietic stem cell transplant pharmacists. *J Oncol Pharm Pract.* 2017. Epub. DOI: 10.1177/1078155217745145
- **Clemmons AB, Alexander M, DeGregory K, Kennedy L.** The Hematopoietic Cell Transplant Pharmacist: Roles, Responsibilities, and Recommendations from the ASBMT Pharmacy SIG. *Biol Blood Marrow Transplant.* 2017. Epub. DOI:10.1016/j.bbmt.2017.12.803.
- **Clemmons AB, Bech CF, Pantin J, Ahmad I.** Acute Kidney Injury in Hematopoietic Cell Transplantation Patients Receiving Vancomycin and Piperacillin/Tazobactam Versus Vancomycin and Cefepime. *Biol Blood Marrow Transplant.* 2017. Epub. DOI:10.1016/j.bbmt.2017.12.799.
- **Gettys SC, Gulbis A, Wilhelm K, et al.** Modified CVAD and modified CBAD compared to high-dose cyclophosphamide for peripheral blood stem cell mobilization in patients with multiple myeloma. *Eur J Haematol.* 2017;98(4):388-392.

Congratulations!

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