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ASBMT Pharmacy Special Interest Group (SIG) Newsletter

Letter from the Chair

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

The first six months as the chair of the Pharmacy Special Interest Group (SIG) for ASBMT have been a huge learning curve for me. What I already knew but has been confirmed is that we have many, many people working hard to bring our members great programming at the BMT Tandem Meetings, continuing education and learning through our monthly SIG literature emails and other endeavors, opportunities for research through our first ever New Investigator Research grant, as well as many other activities.

Another tool that has been extremely helpful is the many responses to our list-serve questions. In March, I had one of my transplant nurse coordinators ask me if other centers were having issues with reimbursement and payment for their transplants performed in the inpatient setting. She asked if I could send an email to the group for query as she knew how helpful my "clinical pearls" could be from these requests. I had no idea that a simple, what I thought was a non-pharmacy question, could lead to such discussion and understanding of many pharmacists including myself about issues related to reimbursement for transplant.

Within hours, I had several emails asking for more details about the problems we were having with approval for inpatient transplant. (You guys do know how to respond quickly!!!) These emails, in addition to other questions, lead to several pharmacists talking to their transplant program directors who then called ASBMT and National Marrow Donor Program (NMDP) to ask for clarification.

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In the end, I think all of us saw a huge push for advocacy to talk to Centers for Medicare & Medicaid Services (CMS) and other legislators to improve the wording in the payment rules for transplant. While we don't know the results of our efforts at this time, I am excited to say that this was a great effort for pharmacists to help lead the way for advocacy in transplant.

This leads to one last observation that I have seen and heard in the past six months, which is questioning which list-serve should I use for asking questions and why do I sometimes get two emails from ASBMT? If you are a member of the ASBMT Pharmacy SIG, you have access to the SIG list-serve which can be sent using pharmacy@list.asbmt.org. This email only goes to members of ASBMT and the Pharmacy SIG and is used to send the monthly literature updates. Another list-serve which was developed before the SIGs were formed is from a Google groups list and is independent of ASBMT. That list-serve includes many other healthcare professionals who like to ask questions of transplant pharmacists. If you have any questions, then please feel free to contact me for further clarification about this or any other SIG topic.

Thanks for all you are doing to help take care of our patients!

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

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.

ASBMT Pharmacy SIG Working Committee Updates

Advocacy and Policy Working Committee

The Advocacy and Policy Working Committee is currently undertaking a number of endeavors in this new term. In the ever-evolving world of social media, the Committee has made significant strides to develop a larger presence on Twitter. The objective is to reach out to ASBMT followers with pertinent information, specifically on an advocacy platform.

The Committee is also looking forward to collaborating with the Program Working Committee for two talks to be given at the annual Tandem meeting. One talk will specifically focus on advocacy and policy awareness while the other is a talk designed to mentor newer presenters on a first-time national presentation.

We have continued in collaboration with the NMDP to further develop patient education tools and are currently awaiting endorsement from both the NMDP and Leukemia & Lymphoma Society (LLS).

The Committee has also been diligently developing a mentorship program in hopes of fostering a community where newer HCT practitioners can reach out to more experienced HCT pharmacists.

Lastly, we are in our final stages of editing a paper detailing our group's findings regarding collaborative practice agreements among HCT centers. We are excited to report on our diverse findings especially as they relate to the pertinent and ongoing issues of obtaining provider status as pharmacists. We look forward to an even more productive fall season.

Research Working Committee

The 2017-2018 Research Working Committee has spent the first half of the year launching the inaugural New Investigator Research Award. Selected applicants have been invited to submit full grant submissions with a winner to be announced in November 2017. The winner will present a short synopsis of their planned research at the 2018 ASBMT Pharmacy Conference. In efforts to increase research collaboration between institutions and other health care disciplines the Committee is organizing a multi-center retrospective analysis of antibacterial prophylaxis with practitioners at M.D. Anderson Cancer Center. We are also discussing potential investigations of anti-viral and biosimilar practices. Another fundamental initiative of the Committee is to foster and promote research within the pharmacy community. We are working to provide updated guidelines and clinical pearls for the Pharmacy Conference Oral Abstract submission process and are discussing with ASBMT leadership avenues to grow submission numbers and standardize review criteria.

Want to become part of an ASBMT Pharmacy SIG Working Committee?

We are seeking enthusiastic and motivated HCT pharmacists! Applications will open in early 2018.

For more information, visit:

http://asbmt.org/about-us/special-interest-

Important Dates

2018 BMT Tandem Meetings
February 21-25, 2018
Salt Lake City, UT

Education Working Committee

The "Beyond Fundamentals of HCT" Course was a success at the Tandem 2017 Annual Conference. There was a record breaking attendance of 90 participants at the 4th edition of this live course. This was a 16-hour course that included new content: pediatrics, busulfan pharmacokinetics, and immune reconstitution along with interactive panel discussions focused on graft-versus-host disease and infectious complications.

In addition to these new offerings, we broadcasted the first webinar in course history in order to include the "Introduction to HCT" session prior to the Tandem Conference; there were 589 registered participants. Based on feedback, interest, and participation from the Tandem conference attendees, the Education Committee will be focusing on the development of future webinars that provide CE.

The Education committee is also developing an augmented 8-hour live Fundamentals Course at the Annual HOPA conference in 2018. There are currently on-line cases based on sessions from the BMT Pharmacist Conference at Tandem in 2014 posted on the ASBMT Pharmacy SIG website. In collaboration with the Programming Committee, we are planning to continue the on-line cases with improvements, beginning with the 2018 Tandem conference content. These improvements will include website presentation and navigation, timing of publishing, and availability of CE. We have been working diligently with Syntaxx and Angie Dahl on our endeavor to increase the availability of continuing education opportunities for HCT pharmacists as well as pharmacy trainees.

We are also continuing to update the Standards of Care

Look for the next *Beyond Fundamentals of Hematopoietic Cell Transplantation (HCT)* Training Course!

This program is held in conjunction with the annual BMT Tandem Meetings. The course provides 16 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 about upcoming program dates, please visit the Pharmacy SIG website:

http://asbmt.org/about-us/special-interest-groups/pharmacy-sig

Important Dates

2018 BMT Tandem Meeting
Abstract Submission
Open now through October 3, 2017

Guidelines and Resource Links are available on the ASBMT Pharmacy SIG website (http://asbmt.org/page/standard-of-care-guidelines-and-resource-links). Our committee plans to be updating this collection of key articles annually.

We are also happy to be adding content specifically targeted toward pediatric practice. With the annual update on the horizon, we will be improving the website navigation of this large detailed body of information.

Program Planning Working Committee

The Program Planning Working Committee has been active in planning for the 2018 BMT Pharmacists Conference at the BMT Tandem Meetings. Topics have been identified and speakers are currently being finalized. In upholding tradition, we will have a strong mix of pharmacist and physician speakers on topics that impact our everyday practice. This year we will introduce a speaking mentorship opportunity in conjunction with the Advocacy and Policy Committee. This program will pair a speaker interested in rising to the national level with an experienced mentor to help guide them through the process. Thank you to the many members of the SIG who have submitted their names to be considered as both speakers and mentors at the upcoming meeting!

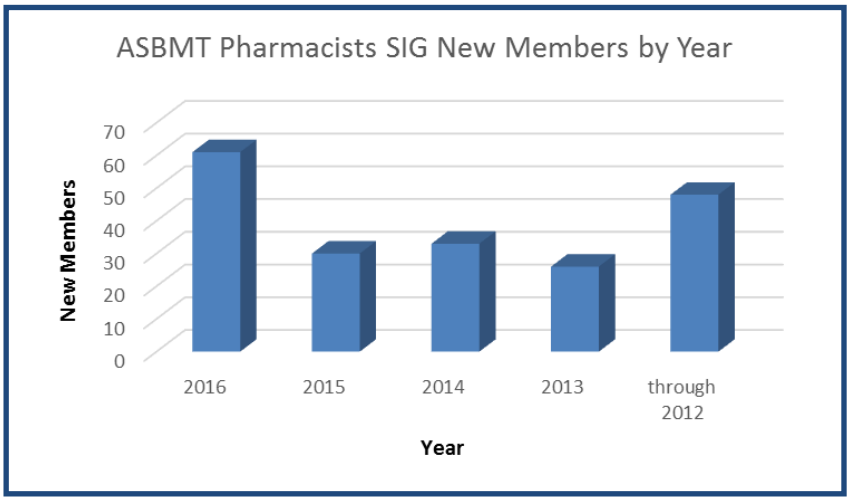
Communications Working Committee

The Communication Working Committee continues to keep the Pharmacy SIG informed of Committee activities and ongoing projects through the biannual newsletter. In addition, the Committee has focused on recognizing our many accomplished HCT pharmacists through member spotlights and highlights.

The Communications Committee 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 ASBMT's Annual Tandem Meeting in our newsletters, as well as monthly summaries of literature affecting HCT practice distributed through the email list-serve. These monthly summaries have been so well-received by our SIG that we are currently considering expanding our distribution to the ASBMT membership at-large.

This year, we have also started contributing to the ASBMT monthly eNews with important SIG updates, so be sure to check it out!

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 Committee 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 encourage SIG members to continue to send us their accomplishments (publications, major awards, etc.) to be highlighted in the newsletters.

We 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 Membership Committee is pleased to announce that membership within the ASBMT Pharmacy SIG continues to increase as we now have 230 members! We continue to be the largest of the ASBMT SIGs. In order to continue to increase membership, the committee continues to send letters to transplant medical directors and PGY2 oncology residency directors inviting their pharmacists to join. The letters highlight the pharmacy SIG benefits for networking and continuing education. We continue to send a welcome letter to new pharmacy SIG members that will help them learn how to get involved with the pharmacy SIG. The committee is especially excited to announce the development of a new award. The **Excellence in Advocacy** award (see the Working Committee Spotlight for details). This makes 3 awards that are now offered by the SIG to recognize the variety of achievements and contributions of our members to the stem cell transplant community. We welcome all to reach out to let us if you have any ideas to make your SIG the best value for our members.

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.

2017 Tandem Update

Teresa Thakrar, PharmD, BCOP

The 2017 BMT Tandem meeting was held February 22-26 in Orlando, FL at the Gaylord Palms Resort and Convention Center. The BMT Pharmacists Conference was held in conjunction with the main meeting and brought together BMT pharmacists from many different backgrounds and practice sites. The conference kicked off with a welcome and update of the ASBMT Pharmacy SIGs' initiatives and accomplishments over the past year.

Pharmacist and physician presenters shared their insights and experiences on challenging cases, unique patient populations, complications associated with stem cell transplant, and novel medications used in the HCT setting. The two-day pharmacist conference was a great venue for networking and sharing exciting research and innovation, including the best pharmacy research abstracts.

Here is a summary of selected presentations from the BMT Pharmacist Meeting:

Thrombotic Microangiopathy in HCT
Sonata Jodele, MD

- Defined and described the pathophysiology of HCT-associated thrombotic microangiopathy (TMA)
- Identified proteinuria and elevated complement levels as poor prognostic markers at diagnosis
- Defibrotide, therapeutic plasma exchange, rituximab, and eculizumab are potential interventions used for HCT-associated TMA

Challenging Cases – Management of Hemophagocytic Lymphohistiocytosis (HLH)
Karissa Kusick Dominick, PharmD, BCOP

- Initial treatment for HLH include a regimen of dexamethasone, etoposide, +/- cyclosporine, and +/- intrathecal methotrexate
- HCT is indicated for patients with familial HLH, relapsed or reactivation of HLH, and severe and persistent HLH. HCT may be considered for patients with CNS disease
- Historically, myeloablative conditioning regimens were used. However, reduced intensity regimens may offer a survival advantage based on retrospective analysis.
- The timing of alemtuzumab administration in reduced intensity regimens relative to day 0 affects the chimerism

Challenging Cases – HCT in CNS Lymphoma
Anthony Proli, PharmD, BCOP, BCPS

- Auto HCT is treatment option for patients with central nervous system (CNS) lymphoma who have relapsed or have had a poor response to initial therapy
- Consider HCT as consolidation therapy for CNS lymphoma due to high relapse rate with consolidation, significant toxicities with current consolidation options, higher chemotherapy doses achievable with HCT, and potentially better tolerability of high dose chemotherapy at a younger age and higher performance status
- More research needs to be done to improve tolerability of conditioning regimen, including decrease infections and auto-GVHD, and maintain remission

2017 Tandem Update (cont.)

Best Pharmacy Abstracts

IV Posaconazole in Pediatric HCT, presented by Ashley Teusink-Cross, PharmD, MBA, BCPS

- Retrospective review to determine the safety and efficacy of IV posaconazole in pediatric patients and establish a dosing regimen for pediatric patients
- Median doses of 10 mg/kg Q24 hours for patients <30 kg and 300 mg Q12 hours for patients ≥30 kg were required to reach a target therapeutic level of >1 mcg/mL for patients
- No patients discontinued posaconazole due to adverse effects

Olanzapine for CINV Prevention in Auto HCT, presented by Theresa Nerone, PharmD

- Retrospective analysis of olanzapine compared to fosaprepitant in patients receiving an auto HCT with busulfan/ cyclophosphamide/etoposide (Bu/Cy/VP) or high-dose melphalan
- For patients who received melphalan, those in the olanzapine group used fewer total breakthrough antiemetics compared to those in the fosaprepitant group
- There was no difference between olanzapine and fosaprepitant for patients who received Bu/Cy/VP

Efficacy of Afternoon Plerixafor Administration Mobilization, presented by Cynthia Elrahi, PharmD

- Retrospective review to determine the efficacy of plerixafor administered for mobilization at 4 pm versus 10 pm in patients with multiple myeloma or lymphoma
- The proportion of patients who achieved a minimal CD34+ cell goal in ≤2 apheresis days, as well as other endpoints, were similar in both the 4pm and 10 pm administration groups

Influence of Body Weight on Melphalan Dosing in Auto HCT, presented by Kendall Shultes, PharmD

- Retrospective study comparing clinical outcomes of melphalan auto HCT for multiple myeloma in obese (weight ≥120% of ideal body weight) versus non-obese patients
- Dose-adjusted melphalan in obese patients was non-inferior to actual body weight in non-obese patients for 3-year event-free survival
- Three-year overall survival, time to neutrophil and platelet engraftment, and length of hospital stay were also similar between obese and non-obese patients

2017 Tandem Update (cont.)

Best Practices in Stem Cell Mobilization

Kathy Hogan Edwards, PharmD, BCPS, BCOP (Medical University of South Carolina)

Amber Diaz, PharmD, BCOP (Oregon Health Sciences University)

Philip Lubanski, PharmD (University of Kansas Hospital)

- Peripheral blood stem cell mobilization strategies were presented from three different institutions
- Reviewed literature on the use of biosimilars in autologous and allogeneic mobilization
- Strategies include: pegfilgrastim 6 mg +/- plerixafor, "double" growth factor +/- plerixafor for patients who fail initial mobilization, variations of risk-adapted plerixafor use based on algorithms, and capping of plerixafor dose and number of doses

The 2018 BMT Tandem meetings will be February 21-25 in Salt Lake City, UT at the Salt Palace Convention Center. Come check out the latest in research and clinical practice, as well as network with colleagues!

Look forward to our next newsletter which will include key abstracts presented at the American Society of Hematology Meeting!

Optimizing Use of Intravenous Immunoglobulin in Hematopoietic Stem Cell Transplantation

Bradley S. Figgins, PharmD; PGY-2 Oncology Pharmacy Resident,
The University of Texas MD Anderson Cancer Center, Houston, TX

Intravenous immunoglobulin (IVIG) is a mixture of polyvalent antibodies fractionated from pooled stores of human plasma. In the setting of hematopoietic stem cell transplantation (HCT), IVIG is frequently used to improve humoral immunity in patients with post-transplant hypogammaglobulinemia, though it has also been employed in the prevention and treatment of acute graft-versus-host disease (aGVHD) and various viral infections.[1] Consensus guidelines endorsed by ASBMT in 2009 recommend against routine IVIG prophylaxis for bacterial infections and suggest use only in those with severe hypogammaglobulinemia (i.e. serum IgG < 400 mg/dL) within the first 100 days post-HCT.[2] An initial dose of 0.5 g/kg/week is suggested for adults, with subsequent individualization to maintain a trough IgG titer > 400 mg/dL. Beyond day +100, the dosing frequency may be increased to every 3-4 weeks for persistent hypogammaglobulinemia.

Despite these recommendations, IVIG use in HCT is marked by significant heterogeneity and uncertainty, reflective of a relatively weak base of supporting evidence. A large meta-analysis published in 2009 failed to demonstrate any benefit of IVIG prophylaxis in terms of documented bacterial infections, CMV infection, infection-related mortality, or aGVHD; instead, increased risks of hepatic veno-occlusive disease and overall adverse effects (e.g., infusion reactions, myalgia, rash) were observed.[3] Notably, a small number of patients undergoing unrelated, HLA-mismatched, peripheral blood, cord blood, or haploidentical transplantation were included; however, a more recent retrospective analysis indicates that these patients likely do not derive additional benefit from prophylactic IVIG.[4]

Multiple cases of dose-related toxicities with IVIG have been reported, including acute hemolysis and various thrombotic events.[5] In response, several updates to the prescribing information for all IVIG products have been made in recent years, including the addition of boxed warnings and language encouraging use at the "minimum dose practicable." This unfavorable risk-to-benefit ratio, in addition to recent IVIG shortages, multi-hour infusions, and high cost have generated an interest to develop strategies to optimize utilization of this resource. A potential method of waste reduction exists in the form of alternative weight-based dosing using ideal (IBW) or adjusted body weight (AdjBW) rather than total body weight (TBW).

"An unfavorable risk-to-benefit ratio, in addition to recent shortages, multi-hour infusions, and high cost have generated an interest to develop strategies to optimize utilization of IVIG."

Prescribing information for commercially available products recommend dosing based upon TBW, the parameter used in clinical trials. The volume of distribution of IVIG ranges from 0.1-0.3 L/kg, indicating that the antibodies primarily reside intravascularly and minimally penetrate into lipophilic tissue.[6] While this information provides rationale for use of dosing weights that are more reflective

of total body water, clinical data supporting such adjustments is currently limited to two small pharmacokinetic analyses in non-HCT populations.

Anderson, et al. performed a correlation analysis examining the relationship between IVIG dose administered (N = 11 doses) and the change in serum IgG titer pre- and post-administration.[7] The correlation coefficient was found to be highest when the dose was normalized according to IBW (r = 0.83) versus AdjBW (r = 0.73) or TBW (r = 0.70). Khan, et al. published a similar analysis evaluating the relationship between IgG trough titer and total IVIG dose administered, normalized according to either TBW or body mass index.[8] Neither of these parameters were found to significantly influence the dose ultimately required to attain goal IgG levels.

The practice of using alternative dosing weights has been acknowledged by several prescribing guidelines and protocols. Public health agencies in the UK, Australia, and Canada recommend use of AdjBW if TBW exceeds 120% of IBW, if not for all patients.[9] No such guidance currently exists in the US, though several academic centers have adopted AdjBW or IBW-based dosing either through protocols or pharmacist-led IVIG stewardship programs.[10]

Currently, the evidence does not support the use of prophylactic IVIG in the setting of HCT. Limited data suggest that IVIG may be considered in severely hypogammaglobulinemic patients with recurrent infections. If used, the dose should be based upon IBW or AdjBW to prevent overexposure and reduce waste. In an increasingly competitive healthcare landscape where greater emphasis is being placed upon quality of care, implementing such prescribing changes may also improve efficiency and enhance patient satisfaction.

References

1. Sokos DR, Berger M, Lazarus HM. Intravenous Immunoglobulin: Appropriate Indications and Uses in Hematopoietic Stem Cell Transplantation. Biol Blood Marrow Transplant. 2002;8:117-130.
2. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for Preventing Infectious Complications among Hematopoietic Cell Transplantation Recipients: A Global Perspective. Biol Blood Marrow Transplant. 2009;15:1143-1238.
3. Raanani P, Gafter-Gvili A, Paul M, Ben-Bassat I, Leibovici L, Shpilberg O. Immunoglobulin Prophylaxis in Hematopoietic Stem Cell Transplantation: Systematic Review and Meta-Analysis. J Clin Oncol. 2009;27(5):770-781.
4. Howell JE, Gulbis AM, Champlin RE, Qazilbash MH. Retrospective analysis of weekly intravenous immunoglobulin prophylaxis versus intravenous immunoglobulin by IgG level monitoring in hematopoietic stem cell transplant recipients. Am J Hematol. 2012;87:172-174.
5. Ammann EM, Jones MP, Link BK, Carnahan RM, Winiecki SK, Torner JC, et al. Intravenous immune globulin and thromboembolic adverse events in patients with hematologic malignancy. Blood. 2016;127:200-207.
6. Koleba T, Ensom MH. Pharmacokinetics of intravenous immunoglobulin: a systematic review. Pharmacotherapy. 2006;26(6):813-827.
7. Anderson CR, Olson JA. Correlation of weight-based i.v. immune globulin doses with changes in serum immunoglobulin G levels. Am J Health-Syst Pharm. 2015;72:285-289.
8. Khan S, Grimbacher B, Boecking C, Sewell W. Serum trough IgG and annual intravenous immunoglobulin dose are not related to body size in patients on regular replacement therapy. Drug Metab Lett. 2011;5(2):132-136.
9. Wimperis J, Lunn M, Jones A, et al. National Health Services clinical guidelines for immunoglobulin use: second edition update, July 2012. Available from http://www.igd.nhs.uk/wp-content/uploads/2016/04/dh_129666.pdf. Accessed June 1, 2017.
10. Rocchio MA, Schurr JW, Hussey AP, Szumita PM. Intravenous Immune Globulin Stewardship Program at a Tertiary Academic Medical Center. Ann Pharmacother. 2016;51(2):135-139.

Plerixafor Use in Pediatrics

Katie Cook, PharmD; PGY-2 Pediatric Pharmacy Resident,
Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, TN

Currently, numerous protocols for the treatment of high-risk pediatric malignancies recommend high-dose chemotherapy followed by subsequent autologous hematopoietic stem cell transplantation.[1] Successful mobilization and collection of peripheral blood stem cells (PBSCs) is dependent upon many factors and can be difficult with the use of G-CSF alone or in combination with chemotherapy. It is estimated between 10-20% of adult patients will fail to mobilize a sufficient number of cells after administration of G-CSF alone. Risk factors for mobilization failure include advanced disease with extensive bone marrow involvement, older patient age, prior use of multiple chemotherapy regimens, extensive prior irradiation exposure, and certain diagnoses, including both Hodgkin and Non-Hodgkin lymphoma and myelodysplastic syndrome.[2]

Plerixafor (Mozobil®) was approved by the FDA in 2008 for use in combination with G-CSF to mobilize hematopoietic stem cells from the bone marrow to the periphery for collection and subsequent transplantation.[3,4] Plerixafor exerts its effect via inhibition of the binding of stromal cell-derived factor-1a to CXCR4, allowing for rapid mobilization of CD34+ cells into the periphery.[4] Plerixafor is commonly used as a second-line agent for stem cell mobilization in adult patients at high risk for mobilization failure.[5] Similar data in pediatric patients have generally been limited and makes appropriate utilization a challenge.

Toledano and colleagues reported their experience with the use of plerixafor in combination with G-CSF following irradiation in a 7 year old child with metastatic medulloblastoma.[5] Following administration of four days of G-CSF, an insufficient quantity (0.3 x 10^6 CD34+cells/kg of stem cells) were collected. Following recovery from a subsequent dose of chemotherapy, the patient received four doses of G-CSF daily with a single dose of plerixafor (240 mcg/kg) administered 10 hours prior to stem cell collection. The patient did not experience any adverse effects and 11.8 x 10^6 CD34+ cells/kg were collected with subsequent successful engraftment.

In 2012, a review of six patients who received plerixafor-based stem cell mobilization therapy after failing mobilization by chemotherapy and four daily doses of G-CSF was published.[5] After failing mobilization with the aforementioned regimen, each patient received four daily doses of G-CSF daily prior to apheresis.[5,6] On the day of collection, Plerixafor (240 mcg/kg) and G-CSF were administered at 10 and 2 hours prior to each collection, respectively. A median of 11.08 x 10^6 CD34+ cells/kg were mobilized in all patients.[6] Three patients experienced successful engraftment, one patient expired due to cardiac arrest, and two patients expired due to spontaneous pneumomediastinum – a pulmonary adverse effect not seen in six control patients treated solely with G-CSF for mobilization. Of note, the patients with pneumomediastinum had previously received irradiation to the thoracic area. The authors concluded that the use of plerixafor in combination with G-CSF showed a mobilization success rate of 100%, though further studies are warranted to investigate the potential association of plerixafor use and development of pneumomediastinum.

A case report was published by Gardellini and colleagues describing a 16 year old with relapsed Hodgkin lymphoma who failed mobilization with G-CSF and chemotherapy.[7] When mobilization was attempted a second time, plerixafor (240 mcg/kg) was added to the regimen, and the first apheresis procedure collected 0.7 x 10^6 CD34+ cells/kg. A second dose of plerixafor was administered, and 1.5 x 10^6 CD34+ cells/kg were collected in the second apheresis session. The patient tolerated the medication well and successfully engrafted at 13 days post-transplant.

"All literature reviewed utilized adult dosing recommendations, which appears to be an appropriate dosing strategy with minimal toxicity and a high mobilization success rate."

In another study, 33 pediatric autologous stem cell transplantation candidates received four daily doses of G-CSF for mobilization, which resulted in insufficient CD34+ cell counts on the planned date of collection. Plerixafor (240 mcg/kg) was added and administered 11-12 hours prior to apheresis.[8] Only 2 patients failed to mobilize a sufficient number of cells after plerixafor, and 4 patients had a suboptimal number of CD34+ cells harvested during the first collection, requiring a second dose of plerixafor. In total, 31 of 33 patients mobilized successfully after 1-2 does of plerixafor, and at publication, engraftment was successful in 23 of 24 patients.

Based on the data reviewed, it appears plerixafor is efficacious for second-line use in pediatric autologous stem cell transplantation candidates who fail to mobilize a sufficient number of CD34+ cells with the use of chemotherapy and G-CSF. Data regarding the use of plerixafor as a first-line agent in pediatric patients with low peripheral CD34+ cell counts prior to apheresis is limited and represents an avenue for further research. All literature reviewed above utilized adult dosing recommendations (240 mcg/kg), which appears to be an appropriate dosing strategy for pediatrics with minimal toxicity and a high mobilization success rate. Given the development of spontaneous pneumomediastinum is a concern based on reports and should be considered when determining utility of this medication on a patient-by-patient basis. Larger, prospective studies are needed to determine the true place in therapy for this medication in the pediatric population.

References:

1. Kessans, Mika R., Mandy L. Gatesman, and Denise R. Kockler. "Plerixafor: A Peripheral Blood Stem Cell Mobilizer." *Pharmacotherapy* 30.5 (2010): 485-92.
2. Mohammadi, S., A. Mohammadi, M. Nikbakht, A. H. Norooznezhad, K. Alimoghaddam, and A. Ghavamzadeh. "Optimizing Stem Cells Mobilization Strategies to Ameliorate Patient Outcomes: A Review of Guide- Lines and Recommendations." *International Journal of Hematology-Oncology and Stem Cell Research* 11.1 (2016): 78-88.
3. Emir, Suna, HA Demir, T Aksu, A Kara, M Ozguner, and B Tunc. "Use of Plerixafor for Peripheral Blood Stem Cell Mobilization Failure in Children." *Transfusion and Apheresis Science* 50.2 (2014): 214-18.
4. "Mobozil (plerixafor)." *Plerixafor*. Genzyme Corporation, n.d. Web. 14 July 2017. <http://products.sanofi.us/Mozobil/mozobil.html>.
5. Toledano, Helen, Anat Yahel, Ian J. Cohen, Isaac Yaniv, and Jerry Stein. "Successful Mobilization, Harvest and Transplant of Peripheral Blood Stem Cells Using AMD3100 and G-CSF following High Dose Craniospinal Irradiation for Medulloblastoma in a Young Child." *Pediatric Blood & Cancer* 54 (2010): 613-15.
6. Hong, KT, HJ Kang, NH Kim, MS Kim, JW Lee, H Kim, KD Park, HY Shin, and HS Ahn. "Successful Mobilization Using a Combination of Plerixafor and G-CSF in Pediatric Patients Who Failed Previous Chemomobilization with G-CSF Alone and Possible Complications

ASBMT Value Assessment in Engineered T-Cell Therapies Meeting Synopsis

Rebecca L. Tombleson, PharmD, BCOP - Advocacy and Policy WC Chair

A meeting was convened earlier this year in Boston on behalf of ASBMT to establish the value of chimeric antigen receptor T-cell (CAR-T) therapies. The meeting featured speakers with expertise in a variety of backgrounds and was convened to answer an over-arching question: How do we determine the value of CAR-T therapy?

The audience was comprised of representatives and leaders from various disciplines, including HCT physicians, health economists, payers, data analysts, patient advocates, pharmaceutical industry, NMDP, FACT, ISCT, and CIBMTR. The objectives were clear from the start: increase understanding of the topics presented, engage in discussion from multiple stakeholder perspectives, identify common goals and challenges, and lastly, establish new collaborations pertinent to CAR-T therapy.

The audience was provided with presentations that broadened awareness of the efficacy and drawbacks of CAR-T therapy from a clinical and financial perspective. The afternoon was dedicated to panel discussions and a special audience-driven breakout session aimed at delineating the pros and cons of existing value assessment frameworks developed by ICER, NCCN, and ASCO. By way of two panel discussions, one with a focus on payer concerns and one dedicated to the operational element of CAR-T implementation, a multi-disciplinary discussion was had. A breakout session involving multi-disciplinary groups then utilized the current value frameworks and attempted to assess the value of CAR-T therapy and determine what elements may not be captured or appropriately delineated within these frameworks. Attendees expressed a range of opinions from excitement at the fruition of this long-anticipated therapy to reservations regarding the complexities of implementation and potential financial burden on patients and institutions.

As representatives of the ASBMT Pharmacy SIG- Advocacy & Policy Working Committee and clinical pharmacy, both I and Ila Maewal Saunders were honored to attend this event. We found opportunities to discuss this unique therapy and the potential benefits and challenges for HCT patients and institutions with our respective multi-disciplinary groups. This therapy has the potential to cause an utter paradigm shift in the way blood cancers are treated and the success with which these patients may be managed comes with key questions that must be answered.

> ***"…we remain poised to approve a therapy that could break every existing mold in the healthcare world."***

In assessing value, care must be taken to account for admission time, toxicities arising from CAR-T therapy, the management of these toxicities and the cost of all of it. Many of the established value frameworks ultimately seek to incorporate the number of quality adjusted life years provided with a specific therapy; this remains an unanswered, yet paramount question. In a volatile healthcare market, with much argument in the last few months regarding blunt access, we remain poised to approve a therapy that could break every existing mold in the healthcare world.

Resident Q & A

What is the role of the bone marrow transplant pharmacist in cellular therapy?

Answered By: Ryan Shaw, PharmD, BCPS, BCOP

Bone marrow transplant (BMT) programs are uniquely equipped to manage cellular therapies. The foundation of transplant relies on immune system modulation balancing graft-versus-tumor and graft-versus-host effects. The continued research and development of chimeric antigen receptor T-cell (CAR-T) will only expand the need for pharmacists trained to manage toxicities of these therapies like cytokine release syndrome (CRS). Bone marrow transplant pharmacists are also familiar with the platform of conditioning/lymphodepleting chemotherapy used in both transplant and CAR-T therapies and the disease states being treated.

The role of pharmacists within cellular therapy has also been recognized on an international level. The Foundation for the Accreditation of Cellular Therapy (FACT) has recently published the First Edition Standards for Immune Effector Cells to provide guidelines for cellular therapy and supportive care. This accrediting body included requirements for HCT pharmacists in the most recent edition of the International Standards for Hematopoietic Cellular Therapy Product Collection, Processing, and Administration and has included many similar stipulations within the cellular therapy standards. Specifically, FACT recommends pharmacists have training in CRS/neurologic toxicity management, be involved in the development of institutional guidelines related to cellular therapy, and earn at least 10 continuing education hours per year related to cellular therapies. Given the paired nature of cellular therapy and bone marrow transplant, both programmatically and by accrediting bodies, BMT pharmacists will be an integral piece of patient care for this exciting and expanding field of cellular therapies.

What new agents are being used in hematopoietic stem cell transplant?

Answered By: D. David Eplin, PharmD, BCOP

While different treatment modalities in HCT have gained recent popularity, such as the use of haploidentical donors for stem cell transplantation, remarkably the chemotherapy and supportive care agents that we use in the field have not changed much over the last several years.

The conditioning regimens used in HCT today remain largely similar to those of the last decade. The area where novel agents have come to fruition, however, are in the maintenance setting and for the treatment of graft-versus-host disease (GVHD). Several agents that are already on the market for other FDA-approved indications have gained popularity in the post-transplant setting to prevent relapse or for treatment of GVHD.

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

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

Resident Q & A (cont.)

One of the most recent classes of chemotherapy agents to gain traction in maintenance therapy are hypomethylating agents. Both azacitidine and decitabine are FDA-approved for the treatment of certain subsets of myelodysplastic syndromes and are also frequently used for the treatment of AML in patients otherwise not suitable for intensive induction induction therapy. However, both agents are more recently being used in patients with myeloid malignancies during the first 100 days post-transplant to prevent relapse. While no major prospective trials have been completed to date, multiple small retrospective studies have shown that these agents are well tolerated and may aide in preventing relapse.

Another agent that has gained popularity in the last few years is the Bruton's tyrosine kinase inhibitor, ibrutinib. This drug is FDA-approved for the treatment of a variety of B-cell disorders, including mantle-cell lymphoma, chronic lymphocytic leukemia/small cell lymphoma (CLL/SLL), Waldenström's macroglobulinemia, and marginal zone lymphoma. Ibrutinib has also recently been used in patients with CLL who have relapsed after allogeneic HCT with results showing promising tolerability and long-term remission rates. It has also shown promising results in a phase Ib/II trial evaluating its use in treatment-refractory chronic GVHD after allogeneic HCT, and a larger phase III trial is currently ongoing. Based on the results of the above phase Ib/II trial, in April 2017 the FDA granted approval of a supplemental indication for ibrutinib for treatment of treatment-refractory chronic GVHD.

Ruxolitinib is a novel inhibitor of Janus Associated Kinases (JAK) 1 and 2, which are involved in many cytokine-mediated functions in the immune system. It is currently FDA approved for the treatment of polycythemia vera (PV) as well as intermediate- and high-risk myelofibrosis. Due to its effects on cytokines and immune-mediated signaling it has been a recent target for research in GVHD, with promising results in multiple phase II trials looking at treatment-refractory acute and chronic GVHD. Another key benefit of ruxolitinib is the steroid-sparing effect for GVHD, as corticosteroids often cause substantial adverse effects. It was granted breakthrough therapy designation from the FDA for the treatment of acute GVHD based on this data.

Have a question or suggestion for our newsletter?

If so, please contact: ASBMTPharmacySIG@gmail.com.

ASBMT Pharmacy SIG Award Spotlight: Lifetime Achievement Award— LeAnne Kennedy, PharmD, BCOP, CPP, FHOPA

Dr. LeAnne Kennedy is one of the clinical pharmacy specialists for hematopoietic stem cell transplantation at Wake Forest Baptist Health (WFBH) in Winston Salem, NC.. LeAnne graduated from Campbell University School of Pharmacy in 1993 and went on to complete her pharmacy practice residency at Wake Forest Baptist Health. After completing her residency training, LeAnne remained at Wake Forest Baptist Health as the clinical pharmacy specialist in hematopoietic stem cell transplantation and has been in that role for over 20 years. She received her board certification in oncology in 2002 and obtained her Clinical Pharmacy Practitioner license in 2013.

Looking back at her 20-plus year career, LeAnne shows no signs of slowing down and remains actively involved in professional organizations and committed to advancing the profession of pharmacy. Within ASBMT, LeAnne is currently the Chair of the Pharmacy SIG Steering Committee, but has also been an active member of the SIG in other capacities, having served as a member or the Chair on the Membership and Awards Committee as well as the Education Committee. LeAnne is also one of the founding members of HOPA and has held numerous leadership positions within that organization. In 2001, LeAnne co-founded the North Carolina Oncology Pharmacist Association with her good friend and colleague, Sally Barbour. As an educator, she still serves as the director of the PGY2 Oncology residency program at Wake Forest Baptist Health. In addition, she holds faculty appointments at Campbell University College of Pharmacy and Health Sciences, UNC Eshelman School of Pharmacy, Wingate University School of Pharmacy, and Wake Forest University School of Medicine. LeAnne also maintains a very active scholarly career as well, authoring or co-authoring over 20 articles to the medical literature and presenting over 30 presentations at various local, regional, and national meetings. In addition to receiving this award, LeAnne's other accolades include receiving the inaugural Award of Excellence from HOPA (2005), the Kappa Epsilon Vanguard Leadership Award (2012), the Campbell University School of Pharmacy and Health Sciences Distinguished Alumni Award (2012), and being recognized in the first class of Fellows within HOPA (2016).

We applaud LeAnne's commitment to mentorship, her patients, and to the profession and asked her: What advice would you give new HCT practitioners?

"For new HCT practitioners, I would recommend to get involved with ASBMT by coming to the meetings and networking and being on a committee. The group of transplant pharmacists is small and very open to providing guidance and mentoring to pharmacists in all practice levels. I don't hesitate to use the Pharmacy SIG list-serve to ask a question and am always pleased to see numerous responses within minutes if not hours. I think it is also important to find another transplant pharmacist to mentor you in your new career. The Pharmacy SIG is working to start a formal process but until then reach out to a pharmacist near you or ask someone to help connect you! If any new practitioner has questions about the ASBMT Pharmacy SIG or transplant in general feel free to send me an email and I will do my best to answer your question or connect you with someone who knows how to better help you."

ASBMT Pharmacy SIG Award Spotlight: Lifetime Achievement Award— LeAnne Kennedy, PharmD, BCOP, CPP, FHOPA

Top: Dr. Kennedy pictured with the past 4 Lifetime Achievement Award Winners (from right to left: Drs. Helen Leather, Joseph Bubalo, Ashley Morris Engemann, LeAnne Kennedy)

Bottom: Dr. Kennedy receiving her Lifetime Achievement award from 2016-2017 Membership WC Chair, Dr. Maurice Alexander

ASBMT Pharmacy SIG Award Spotlight: New Practitioner Award— Ashley Teusink-Cross, PharmD, MBA, BCPS

Dr. Ashley Teusink-Cross is a pediatric BMT pharmacy clinical specialist at Cincinnati Children's Hospital in Cincinnati, Ohio. Ashley completed her PharmD training at the Medical University of South Carolina (MUSC) in Charleston, SC while also simultaneously completing her MBA at the Citadel. Following the completion of her PharmD, she went on to complete her pharmacy practice residency as well as her pediatric pharmacy residency at the Medical University of South Carolina. After completing her residency training, Ashley accepted a position at Cincinnati Children's Hospital, initially starting her career as a clinical pharmacy specialist in critical care and solid organ transplant. In 2012, she joined the Cincinnati Children's Bone Marrow Transplant team, where she remains today.

Since starting her career in HCT in 2012, Ashley has been very active not only within the profession but in the community as well. Within ASBMT, Ashley's been an active member of the Pharmacy SIG and currently is serving as a member of the Program Planning Committee. She also has a strong passion for clinical research and quality improvement, as evidenced by her multiple peer-reviewed publications. She has contributed over 15 articles to the medical literature, but perhaps most notable is her work with pharmacogenetics and extended-spectrum azoles (voriconazole and posaconazole) in the pediatric BMT population. Her research on these topics earned her three "Best of Pharmacy" abstract awards (2013, 2014, 2017) at the ASBMT Tandem Meetings. She also led quality improvement projects at her institution such as the development of a 48-hour in-house medication administration program to help families transition to home, decreasing time to antibiotic administration after first fever in post-HCT patients, and improvement of hypertension management in HCT patients. Although Ashley's professional accomplishments are noteworthy, she was able to combine her passion for fitness with her professional interests by completing a 700 mile bicycle ride over 7 days from Nachez, Mississippi to Cincinnati Children's to benefit HLH research.

We applaud Ashley's commitment to research, her community, and to the profession and asked her: What advice would you give new HCT practitioners?

"The one piece of advice I would give to new practitioners would be to find a professional mentor. Whether this mentor is another pharmacist at your institution, a mentor you find through involvement with ASBMT, or even a physician, I think it can make a huge difference in your career. I am lucky enough to have two physician mentors, one who guides me with my research and another who helps guide me with clinical practice. Establishing these relationships, I believe has allowed me to grow tremendously as a practitioner and a researcher, and made my job more satisfying."

ASBMT Pharmacy SIG Working Committee Spotlight: Membership and Awards Working Committee

The Membership and Awards Working Committee is excited to announce the development of a new award to recognize ASBMT Pharmacy SIG members who have excelled in and display a commitment to patient and/or practice advocacy. The **Excellence in Advocacy Award** will be awarded to an individual who incorporates and promotes the role of the pharmacist in the management of HCT patients.

Advocacy efforts may include, but are not limited to:

- Development of innovative practice models or initiatives that improve the delivery of patient care
- Participation in research that seeks to promote the value and impact of pharmacists in the care of HCT, hematology, and/or oncology patients
- Active involvement in legislative efforts to expand the scope of pharmacy practice
- Engagement in organizational advocacy efforts at the local, regional, or national level.

With all of the amazing contributions our members make in the HCT community, please begin thinking of whom you would like to nominate for the Excellence in Advocacy Award.

In addition to the Excellence in Advocacy Award, we will continue to present the Lifetime Achievement Award and the New Practitioner Award at the annual BMT Pharmacist Conference held in conjunction with the Tandem BMT Meetings.

The Membership and Awards Working Committee remains busy with active recruitment of new members through letters to transplant program directors and PGY2 oncology pharmacy residency directors. With 230 members, the Pharmacy SIG remains one of the largest SIGs in ASBMT! We are hoping to gather additional data on the value of the Pharmacy SIG and conduct a needs assessment to better serve our members. Additionally, we are in discussions with ASBMT to develop a Pharmacy SIG Working Committee online photo directory to aid in networking with colleagues.

As our membership continues to grow, our committee is actively involved in the retention of our current members and welcome any comments or feedback Pharmacy SIG members may have. We look forward to your nominations for the Lifetime Achievement Award, New Practitioner Award, and our newest award, the Excellence in Advocacy Award!

*"With all of the amazing contributions our members make in the HCT community, please begin thinking of whom you would like to nominate for the **Excellence in Advocacy Award**"*

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