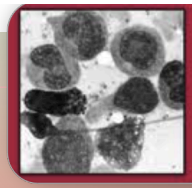
Summer 2014 – Volume 2, Issue 3



ASBMT™
American Society for Blood and Marrow Transplantation

ASBMT Pharmacy Special Interest Group (SIG) Newsletter

Message from the Chair

Jamie F. Shapiro, PharmD, BCOP
Chair, ASBMT Pharmacy SIG

Foundation for the Accreditation of Cellular Therapy (FACT) and Joint Accreditation Committee –ISCT and EBMT (JACIE) Standards

The pharmacy group has achieved a milestone this year with our involvement in the revision of the FACT standards. FACT is a non-profit corporation responsible for the accreditation and inspection of blood and marrow transplant centers. FACT was founded by ASBMT and the International Society for Cellular Therapy (ISCT). Within FACT, appointed committees have developed standards that serve as the foundation for the accreditation process. These standards consist of requirements put forth for the clinical and cellular aspects of hematopoietic stem cell transplantation (HCT). The standards include sections defining the role of practitioners and the services they may provide in addition to the education and training required for their role. The role of the pharmacist in the current 5th edition of the FACT-JACIE standards is minimally stated.

One of the top initiatives of the National Marrow Donor Program (NMDP) System Capacity Initiative (SCI) Pharmacy Group was to demonstrate the important role and utility of clinical pharmacists as part of the multidisciplinary HCT team. Approximately 90% of U.S. HCT centers are FACT accredited, and we believe it is essential to advocate for pharmacists by describing and enhancing the pharmacists' role on the transplant team within the FACT standards. Our goal was to help with recruitment of clinical pharmacists trained in HCT. Over the past year, a pharmacist from the U.S. on behalf of FACT and an international pharmacist on behalf of JACIE participated in conference calls with FACT and JACIE in order to further develop the role of the clinical pharmacist and incorporate this into the new standards. The 6th edition of the FACT-JACIE standards is now under review and includes a thorough description of our role within the HCT team. In order to prevent transplant centers that perform less

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than 50 transplants a year from not being accredited, we were cautious in the wording since those smaller programs may not be able to justify having a full-time clinical pharmacist dedicated to the HCT program and perform all of the duties now listed in the standards. Some of the additions to the standards included training and education of pharmacy personnel, as well as the pharmacists' role in developing guidelines and standard operating procedures, performing therapeutic drug monitoring, and participating in HCT educational activities. We are looking forward to the 6th edition of the FACT-JACIE standards with a more detailed description of our role and the services we can provide for the patient and healthcare team.

Clinical Case Forum (A Multidisciplinary Case-Based Approach to Clinical Conundrums)

I am excited to announce that there is a new venue in which pharmacists who are ASBMT members can obtain assistance and guidance in order to improve patient care. ASBMT has developed a forum for members to pose questions regarding patient care and challenging cases. This is open to all members of ASBMT and is a great way to collaborate and to receive responses and advice not only from peers, but also from experts within the field including physicians, advanced practice professionals, and nurses. The Clinical Case Forum also provides the opportunity to learn about other difficult cases and provide comment. To encourage open discussion among experts in the field of HCT, it is only open to healthcare professionals within HCT. I have personally found the forum a great avenue to learn about intriguing cases and read input from the leading experts throughout the world. Cases and clinical questions are categorized by disease states, patient populations such as pediatrics, and complications such as graft-vs-host-disease (GVHD) and relapse. We look forward to creating a pharmacy group so that all of our questions and cases can easily be searched for by our group as well. This is an excellent way to promote collaboration with other HCT practitioners and keep ourselves up-to-date with issues or innovations in HCT patient care.

If you have any ideas or suggestions for the Pharmacy SIG or our working committees, I encourage you to email us your thoughts at ASBMTPharmacySIG@gmail.com.

Jamie F. Shapiro, PharmD, BCOP
Chair, ASBMT Pharmacy SIG
jamie.shapiro@moffitt.org

Important Dates and Deadlines

2015 BMT Tandem Meetings
The BMT Pharmacists Conference will be held
February 13-14, 2015
Manchester Grand Hyatt, San Diego, CA

Call for Abstracts
The deadline to submit an abstract for the 2015 BMT Tandem Meetings is October 9, 2014

Early registration rates end October 9, 2014

The Fundamentals of HCT Training Course
11th HOPA Annual Conference
March 28-29, 2015
Austin, TX

2016 BMT Tandem Meetings
February 18-22, 2016
Honolulu, HI

ASBMT Pharmacy SIG
Working Committee Updates

Communications & Website Working Committee

The Communications & Website WC continues to expand and improve the content and quality of the Pharmacy SIG newsletter and webpage. We have successfully accomplished our first goal of the year to develop newsletter and webpage editorial guidelines, standardizing the approach for content contributors from a variety of practice backgrounds to share their expertise.

Due to the need for timely updates on recently published literature, the WC has begun utilizing social media such as the BMT Pharmacists Facebook page and BMT Pharmacists Google Group to update our members. Our goal is to educate and to provide updates on treatment and supportive care therapies. The WC also plans to facilitate the use of the ASBMT Clinical Case Forum to provide a medium for SIG members to exchange clinical and technical information and challenges in the HCT clinical setting.

Last but not least, the Communications & Website WC would like to reach out to the next generation of HCT pharmacists and offer career guidance and mentorship. We encourage pharmacy residents and students who are interested in pursuing a career in HCT to submit their questions for an HCT Pharmacist to PharmacySIGCommunications@gmail.com. We also wish to partner with PGY2 Residency Program Directors to support HCT training and direct mentorship to the residents that wish to strengthen HCT knowledge and skills.

Education Working Committee

The Education WC finalized our goals for this year and we are excited to announce our initiatives. The first short-term goal is to develop a resource on the ASBMT Pharmacy SIG webpage with links to standard of care guidelines, landmark papers and educational resources to help both the new and seasoned HCT practitioner. Other short-term goals are to develop an on-line series sharing 2014's recorded BMT Pharmacists Conference presentations along with related cases for members to view and to increase our collaborative work with the Communications WC to expand our educational content.

Our long term goals include developing an online case series with continuing education, developing an ASBMT guideline, and continuing our collaboration with the NMDP to offer the Fundamentals of HCT Training Course. We have been working to secure the next venue for the Fundamentals course and look forward to announcing those details very soon. We always welcome suggestions. Please contact the Education WC at PharmacySIGEducation@gmail.com with any ideas, comments, or concerns.

Call for ASBMT Pharmacy SIG Award Nominations

Nominations are being accepted for: Deadline: **October 1, 2014**

- **The Lifetime Achievement Award**
- **The New Practitioner Award**

Nominees can be either pharmacists or pharmacy technicians, but must be ASBMT Pharmacy SIG members. Please visit http://www.asbmt.org/?page=TandemPharmacy for more details.

Literature Updates

Hematopoietic Cell Transplantation

**King A, Shenoy S. Evidence-based focused review of the status of hematopoietic stem cell transplantation as treatment of sickle cell disease and thalassemia. *Blood*. 2014;123:3089-3094.

- Discussed the indications and expected outcomes for HCT in sickle cell disease and transfusion-dependent thalassemia through an evidence-based review and case presentations.

**Aplenc R, Zhang MJ, Sung L, et al. Effect of body mass in children with hematologic malignancies undergoing allogeneic bone marrow transplantation. *Blood*. 2014;123:3504-3511.

- CIBMTR registry observational study analyzed transplant outcomes of 3687 patients age 2-19 years who underwent allogeneic HCT for hematologic malignancies receiving MAC with cyclophosphamide plus either TBI or busulfan and a bone marrow stem cell source.
- Patients were divided into 5 age-adjusted BMI categories: underweight (<5th percentile), at risk for underweight (5th to < 25th percentile), normal (25th to 85th percentile), overweight (86th to 95th percentile) and obese (> 95th percentile).
- Cumulative incidences of 3-year TRM ranged from 18% in lower BMI group to 28% in higher BMI group (*P*<0.001). Cumulative incidences of 3-year disease relapse ranged from 33% in lower BMI group to 21% in higher BMI group (*P*<0.001).
- There was no significant difference in RFS or OS among the 5 weight groups.

**Pulsipher MA, Chitphakdithai P, Logan BR, et al. Lower risk for serious adverse events and no increased risk for cancer after PBSC vs BM donation. *Blood*. 2014;123:3655-3663.

- Prospective study through the National Marrow Donor Program compared the risk of malignancy and adverse events in unrelated donors who donated BM (N=2726) with donors who donated PBSC (N=6768).
- More BM donors experienced serious adverse events (SAE) compared with PBSC donors (2.38% for BM vs. 0.56% for PBSC, *P*<0.001). SAEs in BM donors were complications of anesthesia and local infections, whereas PBSC donors experienced complications with central venous catheter placement and inflammatory issues.
- There was no difference in risk of cancer excluding non-melanoma skin cancer (*P*=0.722), non-melanoma skin cancer (*P*=0.765), autoimmunity (*P*=0.354), and thrombosis (*P*=0.404) between PBSC donors who received G-CSF and BM donors by 4 years after donation.
- Although SAEs are rare in unrelated donors for allogeneic HCT, BM donors experienced more SAEs compared to PBSC donors, but there was no increased risk found for cancer, autoimmune illness, and thrombosis.

***Armand P, Kim HT, Logan BR, et al. Validation and refinement of the disease risk index for allogeneic stem cell transplantation. *Blood*. 2014;123:3664-3671.

- This registry study utilized a large cohort from the CIBMTR database (N=13,131) to validate the Disease Risk Index (DRI) tool to better predict the outcome of allogeneic HCT based on disease type, cytogenetics, stage of disease and response to induction therapy.
- Using the original DRI, the 2-year OS for this cohort was 64% for low-risk group, 51% for intermediate-risk group, 34% for high-risk group, 24% for very-high-risk group (*P*<0.0001). DRI was the strongest prognostic risk factor, regardless of patient age, conditioning intensity, graft source, or donor type.
- A refined version of the DRI, including the addition of Burkitt lymphoma and other rare disease states, was tested with the current cohort and found similar OS rates as the original DRI: 2-yr OS 66%, 51%, 33%, 23% for low, intermediate, high, and very high risk groups, respectively (*P*<0.0001).
- The validated and refined DRI can be used in patients undergoing HCT for prognostication. It can facilitate the interpretation of single-center, multicenter or registry studies, adjust outcomes data, and stratify patients in clinical trials.

**Chemaly RF, Ullmann AJ, Stoelben S, et al. Letermovir for cytomegalovirus prophylaxis in hematopoietic-cell transplantation. *N Engl J Med*. 2014;370:1781-1789.

- This phase II, multicenter, double-blind clinical trial randomized 131 CMV-seropositive recipients of allogeneic HCT to receive placebo, oral letermovir 60 mg, 120 mg, or 240 mg once daily for 12 weeks following engraftment.
- Incidence of all-cause prophylaxis failure was lower in the 120 mg group (32%) and 240 mg group (29%) compared with placebo (64%) (*P*=0.01 and *P*=0.007, respectively).
- Time to onset of all-cause failure of prophylaxis against CMV infection was shorter in the 240 mg group (*P*=0.002), but not significantly different in other groups compared with placebo.
- Most common adverse events were gastrointestinal disorders (66% in letermovir group vs. 61% in placebo group). Serious adverse events were more common in the placebo group than in all letermovir groups combined (36% vs. 31%).
- Letermovir prophylaxis in recipients of allogeneic HCT was effective at reducing the incidence of CMV infection and had a similar side effect profile as placebo.

***Abu-Dalle I, Reljic T, Nishihori T, et al. Extracorporeal photopheresis in steroid-refractory acute or chronic graft-versus-host disease: results of a systemic review of prospective studies. *Biol Blood Marrow Transplant*. 2014 May 24. [Epub ahead of print] doi: 10.1016/j.bbmt.2014.05.017.

- This is a systematic review of prospective interventional studies evaluating the efficacy of extracorporeal photopheresis (ECP) in adult and pediatric HCT recipients with acute and chronic steroid-refractory GVHD. Nine studies, including 1 randomized controlled trial, totaling 325 subjects were included in the pooled analysis.
- For acute cutaneous GVHD, ECP resulted in the highest pooled ORR of 0.84 (95% CI: 0.75-0.92) followed by acute gastrointestinal GVHD with an ORR of 0.65; similar response rates were seen with chronic GVHD involving the skin and GI tract. ECP did not yield meaningful results in pulmonary chronic GVHD.
- Pooled rates of immunosuppression discontinuation were 0.55 and 0.23 for acute and chronic GVHD, respectively.
- Although there are limited studies, pooled analyses of the prospective studies shows good responses from ECP treatment in the steroid-refractory acute and chronic GVHD setting.

**Chang L, Frame D, Braun T, et al. Engraftment syndrome following allogeneic hematopoietic cell transplantation predicts poor outcomes. *Biol Blood Marrow Transplant*. 2014;20:1407-1417.

- This is a single center retrospective review on engraftment syndrome (ES) in adult and pediatric patients undergoing allogeneic HCT. This has been the largest population evaluated for ES with a total of 927 consecutive allogeneic HCT recipients included in the analysis.
- One hundred nineteen patients (13%) developed ES with a median onset of 10 days after HCT; fever occurred in 100%, rash in 84% and non-cardiogenic pulmonary edema or hypoxia in 54% of patients.
- Systemic corticosteroids were initiated in 79% of ES patients at a median starting dose of 1.1 mg/kg/day; 74% of the patients on steroids progressed to grade II-IV GVHD after a median of 28 days.
- ES patients had a higher cumulative incidence of grade II-IV acute GVHD at day 100 compared with non-ES patients (75% vs. 34%, *P*<0.001), a higher 2-year NRM (38% vs. 19%, *P*<0.001) and a lower 2-year OS (38% vs. 54%, *P*<0.001).
- ES implies a poor prognosis despite early recognition and prompt initiation of steroids.

**Hershman DL, Lacchetti C, Dworkin RH, et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. 2014;32:1941-1967.

- This is the first ASCO guideline on prevention and management of chemotherapy-induced peripheral neuropathy (CIPN).
- There are no agents recommended for prevention of CIPN.
- Duloxetine is given a moderate recommendation for treatment of painful CIPN based on a randomized controlled trial of patients with primarily breast and gastrointestinal malignancies.

**Moreau P, Cavo M, Sonneveld P, et al. Combination of international Scoring System 3, high lactate dehydrogenase, and t(4;14) and/or del(17p) identifies patients with multiple myeloma (MM) treated with front-line autologous stem-cell transplantation at high risk of early MM progression—related death. *J Clin Oncol*. 2014;32:2173-2180.

- This is a study to validate and define a simple prognostic index predicting early MM progression and death within the first 2 years after diagnosis; this study included patients less than 66 years of age who received either bortezomib or lenalidomide induction followed by autologous HCT.
- By using three parameters obtained at diagnosis, International Staging System 3 (ISS3), elevated LDH and adverse cytogenetics [t(4;14) and/or del(17p)], patients with a score of 3 (all previously mentioned parameters) represented 5-8% of MM patients and had a poor prognosis in the previously conducted phase III trials that were analyzed for the validation of this scoring system.
- This model identifies MM patients at high risk of early progression-related death despite current treatment strategies.

***Must read - Landmark publication that affects practice
**Recommend reading - Secondary paper that adds to the literature
*Consider reading - Cursory importance to practice

ASCO, American Society of Clinical Oncology; BM, bone marrow; BMI, body mass index; CI, confidence interval; CIBMTR, the Center for International Blood and Marrow Transplant Research; G-CSF, granulocyte colony-stimulating factor; GVHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; LDH, lactate dehydrogenase; MAC, myeloablative conditioning; MM, multiple myeloma; NRM, non-relapse mortality; ORR, overall response rate; OS, overall survival; PBSC, peripheral blood stem cells; PFS, progression-free survival; RFS, relapse-free survival; TBI, total body irradiation; TRM, transplant related mortality;

Literature search criteria: Publication date- 2014/04/30 to 2014/06/01; Journal- *Biology of Blood and Marrow Transplantation, Blood, Bone Marrow Transplantation, Journal of Clinical Oncology, The New England Journal of Medicine, Pediatric Blood & Cancer*

Resident and Student Questions for an HCT Pharmacist

Question: Do you follow up on patients' adherence to their medication regimens?

Answer:

Cathryn Jennissen, PharmD, BCOP
University of Minnesota Children's Hospital

Once a patient is discharged from the hospital, it is up to the patient and/or caregiver to administer medications and ensure adherence. This can be a very overwhelming process especially early after discharge. As such, the pharmacist working in our outpatient BMT clinic checks in with all patients during each visit the first week after discharge. Our patients are given an outpatient medication schedule during discharge teaching and they are instructed to bring it to each clinic visit. The clinic pharmacist goes through this schedule with them again and reemphasizes teaching points. We also utilize the teach-back method, in which we ask the patient and caregivers questions about their medication therapy. We ask about adherence at each visit as well. We know that medication doses can get missed, but we encourage the patient to be open and honest. If a patient misses doses on a routine basis, we try to work together to make their medication schedule more feasible and more fitting to their lifestyle. Medication reconciliation is performed at each clinic visit to ensure that the patient's medication schedule is up-to-date, as doses are often changing and medications are started or discontinued. With some patients and caregivers, we have taken on the task of filling their medication box once a week. This has greatly improved adherence in some patients.

Question: Are there different counseling points for the different types of transplantation?

Answer:

Cathryn Jennissen, PharmD, BCOP
University of Minnesota Children's Hospital

There are definite differences in counseling a patient who received an autologous transplant versus an allogeneic transplant. However, there are common counseling points for any HCT patient including education on what a medication is for, how to take it, common side effects, and encouraging adherence.

For patients undergoing allogeneic transplant, a large focus is placed on the immunosuppressive agents, including cyclosporine, tacrolimus, and sirolimus. It is important that the patient fully understands that these medications are necessary to prevent graft-vs-host-disease (GVHD), and it is very important to take as prescribed. Additionally, the patient should be informed that their blood levels will be checked frequently (typically once a week) and their medication dose may change as a result. Moreover, these medications have common side effects, including hypertension and hypomagnesemia, which may result in the patient taking additional medications to control these issues.

Prophylactic antimicrobials are a part of the medication regimen in both types of transplant, given the high risk of infection. The allogeneic population typically receives antimicrobials for 6-12 months, while autologous patients receive 3-6 months of prophylaxis. Patients and their caregivers are counseled on the "typical" infections that can occur in the HCT patient, including but not limited to cytomegalovirus (CMV) reactivation, herpes simplex virus (HSV) reactivation, bacteremia, pneumocystis carinii pneumonia (PCP), and fungal infections including yeast and mold. The patient is educated to contact the HCT team immediately at any sign of infection, such as fever, cough, change in bowel function, development of a rash, or change in respiratory function.

Dr. Jennissen is a clinical pediatric pharmacist in the pediatric HCT unit and outpatient clinic at the University of Minnesota Children's Hospital. Located in Minneapolis, MN, the pediatric HCT group performs approximately 75 pediatric allogeneic and 15 pediatric autologous transplants per year.

Question: Do you have a lot of patient interaction?

Answer:

Adam Melaragno, PharmD
Barnes-Jewish Hospital/Washington University Medical Center

As an inpatient HCT clinical pharmacist, the majority of my interaction with patients relates to education

regarding chemotherapy and transplant conditioning regimens. Upon admission, I meet with patients and their families to discuss dosing schedule, possible drug toxicities, monitoring, and supportive care issues. This is a great opportunity for patients and their caregivers to ask any medication-related questions. I also use this time to obtain an accurate medication history to ensure we have continued the appropriate home medications and are better prepared to identify and manage drug interactions. Having an accurate allergy list is crucial, so I use this introductory meeting to discuss and clarify allergy information with patients, especially with regards to antimicrobials. Most patients require antimicrobials at some point during their transplant admission, and it helps to know what their prior allergy or intolerance was when deciding on appropriate treatment.

Throughout the hospital stay, I work with patients who are having issues with nausea, vomiting, or pain to devise a plan of care to improve their symptoms. When patients are approaching discharge, I meet with them to discuss new medications such as immunosuppressive agents and antimicrobial prophylaxis.

As pharmacists, our ultimate responsibility is to be a patient advocate. To achieve this responsibility, communicating with patients is key. Personally, it adds to my job satisfaction and developing relationships with patients makes the hard work well worth it!

Question: Are there different counseling points for the different types of transplantation?

Answer:

Adam Melaragno, PharmD
Barnes-Jewish Hospital/Washington University Medical Center

There are certainly different points of discussion for patients undergoing different types of HCT. In the inpatient setting, I usually focus my conversation on the acute issues and allow the outpatient team to focus on long-term care and follow-up.

For patients undergoing an autologous transplant, I first review the schedule and toxicity of the conditioning regimen. The two most common conditioning regimens we use are high-dose melphalan for patients with multiple myeloma and BEAM (carmustine, etoposide, cytarabine, and melphalan) for patients with lymphoma. Both regimens are associated with GI toxicities, including diarrhea and mucositis, so we discuss ways to prevent and manage these toxicities with anti-emetics and cryotherapy. The frozen stem cells are preserved with dimethyl sulfoxide (DMSO), which has unique toxicities including taste alterations, flushing, shortness of breath, and headache. Finally, I discuss the risk of infection and the importance of antimicrobial prophylaxis.

For patients undergoing an allogeneic transplant, depending on the conditioning regimen, there are many points of discussion that are beyond the scope of this newsletter. However, the main difference for allogeneic transplant recipients is the need for immunosuppression to prevent graft-vs-host-disease (GVHD), which is a common and potentially fatal complication post-transplant. Therapeutic drug monitoring is important for many of these immunosuppressants, including tacrolimus, cyclosporine, and sirolimus. It is important to assure patients understand how to take their prescriptions and to inform them that there are risks for interactions with other prescription and over the counter medications. Because of the chemotherapy and intense immunosuppression, these patients are at high risk for a variety of infections. Most will be maintained on viral, fungal, and pneumocystis prophylaxis for approximately six months or until no longer receiving immunosuppression, and will be periodically screened for reactivation of viruses, including cytomegalovirus (CMV) and Epstein-Barr virus (EBV), and herpes simplex virus (HSV).

Dr. Melaragno is an inpatient hematologic malignancies and HCT clinical specialist at Barnes-Jewish Hospital/Washington University Medical Center. BJH is located in St. Louis, MO and performs approximately 200 allogeneic and 250 autologous transplants each year.