Winter 2016 – Volume 4, Issue 1

ASBMT Pharmacy Special Interest Group (SIG) Newsletter

ASBMT Pharmacy SIG Working Committee Updates

Advocacy and Policy Working Committee

The Advocacy and Policy Working Committee began the year by updating our charter to increase our membership from 7 to 9 members, one of which is a non-voting Policy Advisor. The Policy Advisor is instrumental in the development of communications to keep the Pharmacy SIG membership up-to-date on current legislation and advocacy opportunities. Examples of these communications include "How to Track a Bill", "5 W's of Advocacy" and "Advocacy for Pharmacists Provider Status."

The committee developed a Collaborative Practice Agreement (CPA) survey. The results were submitted as an abstract for 2016 BMT Tandem Meeting, and publication is in progress. We will continue the tradition of supporting our Pharmacy SIG efforts through Letters of Recognition that will be sent to the direct supervisors of the Steering Committee membership and Working Committee chairs for the 2015-2016 term. The direct supervisors of the Working Committee members will receive an email version of the Letter of Recognition.

We are actively engaged with our Education Working Committee members on two exciting projects. Documents are being developed in collaboration with the National Marrow Donor Program (NMDP) in defining the role of the HCT pharmacist and HCT Pharmacist-Patient Education. The goal is to make the documents available on the NMDP website. We are also exploring a formal

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mentorship program to assist our new HCT pharmacist colleagues in navigating their entry into our HCT specialty.

We hope to have a Pharmacy SIG brochure out by early 2016. This will be utilized by the ASBMT as a mechanism to highlight the efforts and value of the Pharmacy SIG to our patients and healthcare providers in hopes of sustaining and growing education grant support. The working committee is excited to continue our current efforts and looks to find new sustainable initiatives to support the role of the HCT pharmacists.

Membership and Awards Working Committee

The Membership and Awards Working Committee is pleased to announce the ASBMT Pharmacy SIG membership continues to increase, as we now have over 150 members. This is a 10% increase in membership from last year. In order to increase membership, the committee has drafted a letter to medical directors at blood and marrow transplantation centers and PGY2 oncology residency directors highlighting the Pharmacy SIG benefits for networking and continuing education. We have also developed a welcome letter for new Pharmacy SIG members to help them become involved with the Pharmacy SIG. The committee is excited to recognize our new award winners for the New Practitioner and Lifetime Achievement awards at the annual BMT Tandem Meeting in Hawaii. On a final note, we are looking for ways to utilize social media to promote the Pharmacy SIG and also to highlight the activities of different HCT pharmacists and achievements. The Membership and Awards Working Committee continues to be busy and welcomes any thoughts for future activities for the committee.

Research Working Committee

The Research Working Committee has spent the past year developing infrastructure to promote research among members of the ASBMT Pharmacy SIG and for the field of HCT. The committee reviewed research submissions to the 2016 BMT Tandem Meeting and selected abstracts for oral and poster presentations. In addition, the committee created a list of research grants aimed for pharmacists and created a link on the ASBMT Pharmacy SIG website as a resource to promote grant-funded HCT research conducted by pharmacists. Furthermore, the committee added all abstracts presented at the Pharmacists Conference at the BMT Tandem Meetings of the past 5 years to the Pharmacy SIG website. This year, the committee has started working on the development of the ASBMT Pharmacy New Investigator Research Grant Award that is intended to provide support for a HCT pharmacy practice research project. The scope of the research project may include clinical, laboratory or translational science, pharmacoeconomics, health services and policy, or humanistic research related to hematopoietic cell transplantation.

Communication and Website Working Committee

The Communications Working Committee continues to promote the dissemination of information in relation to the Pharmacy SIG and HCT literature. The committee is also working with ASBMT to provide contents and improvements to the Pharmacy SIG webpage.

Important Dates and Deadlines

2017 BMT Tandem Meetings
February 22-26, 2017
Orlando, FL

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

The committee recently surveyed the Pharmacy SIG membership to evaluate the usefulness of the Pharmacy SIG Newsletter and the Literature Updates. Results showed that a majority of members found the content in these publications to be helpful in updating them on the activities of the SIG and pertinent publications. The Pharmacy SIG Newsletter continues to be published on a triannual schedule, and the Literature Updates are published monthly. The committee has finalized guidelines for newsletter contributors, with additional educational content now being included with each issue of the newsletter.

Education Working Committee

The Education Working Committee held an 8-hour "Fundamentals of Hematopoietic Cell Transplant" educational program following the annual HOPA meeting in Austin, Texas in March 2015. Sixty-seven individuals attended this program and the evaluations were very positive. We appreciate the efforts of Melisa Stricherz and the Education Working Committee, NMDP, and Syntaxx Communications in making this program a success. We plan to offer a more comprehensive 16-hour course in conjunction with the 2017 BMT Tandem Meetings.

Progress has also been made in developing a resource document that will include standard of care references relevant to the practice of stem cell transplantation. We expect this to be available on the ASBMT Pharmacy SIG webpage later this winter.

Program Planning Working Committee

The Program Planning Working Committee has been working diligently to develop a two-day Pharmacists Conference at the 2016 BMT Tandem Meetings in Honolulu, Hawaii. During this conference, leaders within the field of HCT provided expert perspective on the management of this complex patient population using an evidence-based approach. Thirteen hours of continuing education credit was offered. New in 2016 was a two-hour Combined Clinical Practice Session offered at the start of the BMT Pharmacists Conference. This session was a collaborative effort between the Pharmacy, Advanced Practice Professionals and Nursing SIGs. A speaker sponsored by each SIG presented a topic related to HCT survivorship.

The BMT Pharmacists Conference was held on Saturday, February 20th and Sunday, February 21st, 2016. To view the full program agenda, please go to:

https://bmt.confex.com/tandem/2016/meetingapp.cgi/Program/1120

Send questions or comments to the ASBMT Pharmacy SIG Leadership:

General SIG - ASBMTPharmacySIG@gmail.com

Education and Program Planning WC - PharmacySIGEducation@gmail.com

Communications WC - PharmacySIGCommunications@gmail.com

Resident and Student Questions for an HCT Pharmacist

Answered by:
Cathryn Jennissen, PharmD, BCOP
University of Minnesota Masonic Children's Hospital

Question: What type of medication interventions do you make?

Answer:

Patients that undergo hematopoietic stem cell transplantation (HCT) are on multiple scheduled medications. As such, there are numerous opportunities to make medication interventions for each patient. I perform a thorough medication profile review on a daily basis for each patient to assess for duplicate drug therapy, drug interactions, renal/hepatic dose adjustments, accurate dose per indication, length of therapy, therapeutic drug monitoring, adverse medication reactions and so forth. I am often recommending dose adjustments based on drug interactions, particularly with calcineurin inhibitors and azoles. There are multiple drug levels to evaluate each week as well, most commonly being the calcineurin inhibitors. Based on the results, I make recommendations for dose adjustments as appropriate. We also evaluate drug levels with azoles, vancomycin, aminoglycosides, anticonvulsants, and busulfan chemotherapy as appropriate. Because a majority of our patients require TPN therapy at some point during their HCT course, I am frequently making recommendations to the TPN electrolyte content based on lab results. HCT patients are very immunosuppressed, and many of them develop infections during the peri-transplant period. I work with the team to determine the best antimicrobial agent to treat the infection based on the microbe, susceptibility, and location of infection. Additionally, HCT patients are also at high risk of developing renal insufficiency due to exposure to multiple nephrotoxic medications and fluid balance issues that are frequently encountered during the transplant process. As such, renal dose adjustments are common interventions done in my practice.

I also work with the BMT physicians to determine the best conditioning regimen for patients prior to their admission for HCT. The recommendations/ interventions that I most commonly make are dose adjustments to the chemotherapy based on the patient's pre-existing renal dysfunction, obesity, and/or history of adverse reactions. In addition to the chemotherapy, I will assess the patient's risk for infection, history of nausea and vomiting, and history of opioid use. Based on this assessment, I will make recommendations/interventions, as appropriate, with regards to prophylactic anti-infectives that will best suit the patient, as well as preferred antiemetics and opioids.

Answered by:
Adam Melaragno, PharmD, BCOP
University of Rochester Medical Center

Question: What strategies do you employ to stay up to date in your field?

Answer:

This is a great question, and I believe that many pharmacists would answer this is many different ways. For the oncology pharmacist, this question is especially pertinent given the rapidly evolving field, new therapies, and increased understanding of each malignancy. Although this can sometimes be a daunting task, it is

also what drew me to oncology pharmacy practice. Each day is different and I continually learn.

There are many resources that are available to help HCT pharmacists stay updated in the field. The first step is to join a professional organization, such as ASBMT, in order to take advantage of and participate in many learning opportunities. The annual BMT Tandem Meetings is an excellent way to attend live programming and network with other pharmacists in the field. Also provided through many professional organizations are listservs or forums where questions can be posed and important updates in the field can be shared. Many organizations also publish newsletters which contain therapeutic updates, clinical controversies, and drug class overviews. The ASBMT Pharmacy Special Interest Group also publishes monthly literature updates that summarize transplant-related primary literature.

Another strategy for continued learning is to sign up to receive table of content alerts through individual journals. This allows the learner to read articles that are pertinent to his/her practice without actively searching. These alerts are often able to be customized to specific disease states and clinical areas.

Most hospitals and pharmacy schools offer learning opportunities as well, in the form of lecture series, continuing education presentations, journal clubs, or patient case presentations. These offer unique opportunities to learn from and collaborate with other healthcare providers within your institution.

I believe the most important and most beneficial method of staying up-to-date in the field is to get involved. Whether that be at the local hospital level by updating protocols, order-sets, and treatment plans, or on a state, regional, or national level by joining professional organizations and contributing to their work. Each opportunity provides learning and encourages you to access the most up-to-date information in the field.

Dr. Jennissen is a clinical pediatric pharmacist in the pediatric stem cell transplant unit and outpatient clinic at the University of Minnesota Masonic Children's Hospital, Fairview. Located in Minneapolis, MN, the pediatric stem cell transplant group at the University of Minnesota performs approximately 80 transplants per year.

Dr. Melaragno is an inpatient clinical pharmacy specialist in HCT at the University of Rochester Medical Center. The HCT program in Rochester, NY, performs approximately 150 transplants per year.

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

We would like to answer them!
Please email any questions to the ASBMT Pharmacy SIG Communications Working Committee: PharmacySIGCommunications@gmail.com

Literature Updates from the American Society of Hematology (ASH) Annual Meeting 2015

***Stone RM, Mandrekar S, Sanfor BL, et al. The multi-kinase inhibitor midostaurin (M) prolongs survival compared with placebo (P) in combination with daunorubicin (D)/cytarabine (C) induction (ind), high-dose (C) consolidation (consol), and as maintenance (maint) therapy in newly diagnosed acute myeloid leukemia (AML) patients (pts) age 18-60 with *FLT3* mutations (muts): an international prospective randomized (rand) p-controlled double-blind trial (CALGB 10603/RATIFY [Alliance]). *Blood.* 2015;126(23):Abstr 6.
https://ash.confex.com/ash/2015/webprogram/Paper80269.html

- A multicenter, phase III, randomized, double-blind, placebo controlled study comparing induction chemotherapy (daunorubicin/cytarabine) and consolidation (high-dose cytarabine) + midostaurin (PKC412) or placebo in 717 newly diagnosed *FLT3* mutated Acute Myeloid Leukemia (AML) patients < 60 years of age.
- Overall survival (OS) was the primary endpoint, with a 4-year OS rate of 51.4% (M) compared to 44.2% (P) (1 sided log-rank p-value: 0.0074). The median OS was 74.7 months (M) and 25.6 months (P), a 23% reduced risk of death in the midostaurin arm.
- Of the 409 (57%) patients in the study that went on to receive a hematopoietic cell transplant (HCT), 63.8% of M patients and 55.7% of P patients were alive at 4 years. Treatment with M increases OS after HCT in CR1 (HR: HCT in CR1 0.61; HCT outside CR1 0.98).
- There was a similar number of grade 5 adverse events reported across both arms, with a rate of 18 (5%) in the M treatment group and 19 (5.3%) in the P group. Grade III-IV non-hematologic events seen in ≥ 10% of patients were also similar, with rash/desquamation seen more commonly in the M treatment arm (M: 13%, P: 8%, p-value 0.02).
- Midostaurin improves OS when added to chemotherapy in newly diagnosed patients aged 18-60, with ITD and TKD *FLT3* mutant AML. It has OS and event free survival (EFS) benefits seen in both uncensored and censored analyses, despite such a high transplant rate seen in this study. There was a similar safety profile in each arm. Based on the results of this study, midostaurin added to chemotherapy represents a new standard of care.

***Townsley DM, Dumitriu B, Scheinberg P, et al. Eltrombopag added to standard immunosuppression for aplastic anemia accelerates count recovery and increases response rates. *Blood.* 2015;126(23):Abstr LBA-2.
https://ash.confex.com/ash/2015/webprogram/Paper87452.html

- This phase II, single center trial evaluated the addition of eltrombopag to immunosuppressive treatment (IST) with horse antithymocyte globulin (hATG) and cyclosporine (CSA) for treatment-naïve severe aplastic anemia (SAA) in 88 patients aged ≥ 2 years using a triple cohort design.
- The primary endpoint of the protocol was complete response (CR) at 6 months. There was a CR rate of 37% seen in the three combined treatment cohorts, compared to 12% in the historical comparator group. The highest CR rate was achieved in the cohort receiving eltrombopag 150 mg starting day 1 through 6 months in addition to standard IST (CR 60%, p<0.001).
- Overall hematologic response (OR) at six months was 86% in all patients, compared to 63% historically. Again, the cohort receiving eltrombopag beginning on day 1 had the highest OR rate at 95%. Few grade III-IV events were attributed to eltrombopag. Two patients stopped eltrombopag therapy due to severe cutaneous reactions and 10% of eltrombopag-treated patients had grade II-III transaminase and bilirubin elevations. No increased fibrosis on bone marrows was seen during this study.

- Eltrombopag increases both ORs and CRs in treatment-naïve SAA. Eltrombopag therapy was associated with an increased number of CD34+ cells, robust neutrophil and platelet count recovery and transfusion independence within 1-2 months. Immediate introduction of eltrombopag with IST had the highest success rates. Longer follow-up will be required to assess long-term success and relapse rates after eltrombopag + IST.

***Durie B, Hoering A, Rajkumar SV, et al. Bortezomib, lenalidomide and dexamethasone vs. lenalidomide and dexamethasone in patients (Pts) with previously untreated multiple myeloma without an intent for immediate autologous stem cell transplant (ASCT): results of the randomized phase III trial SWOG S0777. *Blood.* 2015;126 (23):Abstr 25.
https://ash.confex.com/ash/2015/webprogram/Paper79014.html

- This phase III, randomized, multicenter trial compared bortezomib, lenalidomide and dexamethasone (VRd) to lenalidomide and dexamethasone (Rd) in 474 previously untreated multiple myeloma patients evaluable for survival endpoints.
- Median progression free survival (PFS) was 43 months (VRd) versus 30 months (Rd) and median OS was 75 months (VRd) versus 64 months (Rd). The OS was improved for VRd vs Rd (HR=0.666; two-sided log-rank p-value=0.01114). The overall response rate (ORR) for VRd was 71.07% versus 63.79% for Rd.
- The adverse events were well balanced between the two groups. The most commonly reported hematologic events (≥ grade 3 and at least possibly attributable to therapy) were lymphopenia (VRd=23%; Rd=18%), neutropenia (VRd=19%; Rd=21%) and thrombocytopenia (VRd=18%; Rd=14%). The most common non-hematologic adverse events (≥ grade 3 and at least possibly attributable to therapy) were fatigue (VRd=16%; Rd=14%), sensory neuropathy (VRd=23%; Rd=3%), and hyperglycemia (VRd=7%; Rd=11%).
- Both PFS and OS are significantly improved with the addition of bortezomib to lenalidomide + dexamethasone. VRd induction is a potential new standard of care.

**Attal M, Lauwers-Cances V, Hulin C, et al. Autologous transplantation for multiple myeloma in the era of new drugs: a phase III study of the Intergroupe Francophone De Myelome (IFM/DFCI 2009 Trial). *Blood.* 2015;126(23):Abstr 391.
https://ash.confex.com/ash/2015/webprogram/Paper78452.html

- A prospective, randomized trial comparing conventional dose treatment lenalidomide, bortezomib, and dexamethasone (RVD) to RVD with autologous cell transplant (ASCT) in 700 previously untreated patients, to determine if transplant was still necessary in the initial management of patients aged ≤ 65 years.
- For the primary endpoint of PFS, ASCT was found to improve PFS (stratified p value for log-rank test <0.0002). The 3-year post-randomization PFS rate was 61% in the transplant arm versus 48% in the RVD arm.
- OS 3 years post-randomization was extremely high (88%) and similar between the two study groups. The transplant arm had a significantly higher CR rate compared to the RVD arm: 58% vs. 46%, respectively (p<0.01). 80% of patients in the transplant arm achieved minimum residual disease (MRD) negativity, compared to 65% in the RVD arm (p=0.001).
- Grade III-IV adverse events were seen more commonly in the transplant arm; neutropenia (89% vs 31%), thrombocytopenia (78% vs 9%) and infections (18% vs 10%).
- ASCT should remain a standard of care for young patients with de novo myeloma. Transplantation was associated with an acceptable treatment-related mortality (TRM) (1.4%), improved rate of MRD negativity, and improved 4 -year PFS (47% vs 35%, p<0.001). Longer follow up is required to draw any conclusion concerning OS since 4 – year OS is similar in both arms (80% vs 83%) and the number of deaths is still so low in both arms.

*Fiala MA, Schwab D, Vij D, et al. A Randomized trial of tbo-filgrastim versus filgrastim for autologous stem cell mobilization in patients with multiple myeloma or non-hodgkin lymphoma. *Blood.* 2015;126(23):Abstr 516. https://ash.confex.com/ash/2015/webprogram/Paper85848.html

- A prospective, single center, randomized, open label phase II non-inferiority trial comparing the peripheral blood (PB) $CD34^+$ counts, $CD34^+$ apheresis yield, toxicity, and post-ASCT engraftment in 100 patients mobilized with tbo-filgrastim compared to filgrastim.
- The primary objective of the study was day 5 (first day of apheresis) $CD34^+$ cells/kg yield in adult patients diagnosed with multiple myeloma (MM) or non-hodgkin's lymphoma (NHL) undergoing their first ASCT. The median $CD34^+$ yield on day 5 was similar between the two groups at 11.3 x 10^6 cells/kg for tbo-filgrastim and 10.8 x 10^6 cells/kg for filgrastim (p=0.443).
- 82% of patients in both arms reached the collection goal after one day of apheresis. Both treatment arms had similar toxicity. Post-ASCT engraftment was equivalent between the two groups with a median neutrophil engraftment at 12 days and median platelet engraftment at 17 days.
- Tbo-filgrastim appears to be similar to filgrastim for ASCT mobilization in patients with MM or NHL.

*Showel MM, Fuch EJ, Varadhan R, et al. Related nonmyeloablative haploidentical (mini-haplo) blood or marrow transplantation (BMT) with high-dose post-transplant cyclophosphamide (PTCy) for acute myeloid leukemia (AML): donor age impacts outcome. *Blood.* 2015;126(23):Abstr 151. https://ash.confex.com/ash/2015/webprogram/Paper83765.html

- This retrospective, single center review of all adult patients that received a mini-haploidentical HCT for high-risk AML studied the impact of donor age on outcome.
- The median age of the 93 AML patients was 54 years, and half of the donors were children of the patients. This review uncovered that the patient age was inversely proportional to donor age, and older donors (not patients) were associated with a higher rate of graft failure.
- The 11 patients that developed graft failure received allografts from donors that were older, median age 49 versus 38 years (p=0.03) and received allografts with significantly fewer $CD34^+$ cells, median of 2.5 x 10^6 cells/kg compared to 4.5 x 10^6 cells/kg (p=0.01).
- When comparing donor age < 40 versus ≥ 40, the incidence of graft failures was 2% vs 22% (p=0.003). Patient age did not have a significant impact on survival. For patients with donors ≤ 55 years, median OS was 63 months compared to 13 months (p=0.14).
- In conclusion, older donors are associated with poor graft quality, increased graft failure, and a trend towards decreased OS. Mini-haplo HCT offers a potentially curative option for poor-risk AML patients lacking a matched donor, and no AML patients should be denied the procedure for lack of a suitable donor. Donor age should be one of the characteristics taken into consideration when choosing a potential donor and further prospective studies should be completed to confirm this data.

**Gaballa S, Ge I, El Fakih RO, et al. Results of a two-arm phase II clinical trial using post-transplantation cyclophosphamide for prevention of graft-versus-host disease in haploidentical and mismatched unrelated donors hematopoietic stem-cell transplantation. *Blood.* 2015;126 (23):Abstr 152. https://ash.confex.com/ash/2015/webprogram/Paper82529.html

- A prospective, non-randomized, parallel, phase II clinical trial investigating the safety and efficacy of graft-versus-host disease (GVHD) prophylaxis with post-transplant cyclophosphamide (PTCy), tacrolimus (FK) and mycophenolate mofetil (MMF) between haploidentical (HAPLO) versus 9/10 matched unrelated donor (MUD) transplantation, in the setting of a uniform melphalan-based reduced-intensity conditioning (RIC) regimen.
- The primary outcome was to compare the non-relapse mortality (NRM) at day +100: 1-year cumulative incidence of NRM was 21% in the HAPLO arm and 31% in the 9/10 MUD arm, while the 1-year relapse rate was 19% and 25% in the two groups, respectively.

- The 1-year OS and PFS were 70% and 60% HAPLO, respectively, and 60% and 47% MUD, respectively. The cumulative incidence of grade II-IV acute GVHD (aGVHD) and III-IV aGVHD at day 100 were 28% and 3% HAPLO, respectively, versus 33% and 13% MUD, respectively; the 2-year cumulative incidence (CI) of chronic extensive GVHD was 13% HAPLO and 14% MUD. Primary graft failure occurred in two patients in the HAPLO arm and one patient in the 9/10 MUD arm.
- This study establishes PTCy, FK, and MMF as an effective strategy for GVHD prophylaxis in mismatched transplantation using both haploidentical and mismatched unrelated donor sources.

**Damlaj M, Alkhateeb HB, Partain DK, et al. Fludarabine busulfan compared to fludarabine melphalan Is associated with increased relapse risk in reduced intensity conditioning transplant despite pharmacokinetic dosing. *Blood.* 2015;126 (23):Abstr 736.
https://ash.confex.com/ash/2015/webprogram/Paper79843.html

- A single center, retrospective study comparing transplant -related outcomes of fludarabine busulfan (FB) using intravenous (IV) busulfan targeted to the area under the curve (AUC) to fludarabine melphalan (FM) in 134 patients with AML or myelodysplastic syndrome (MDS).
- There was a statistically significant difference in 2 year relapse incidence and PFS among the FB and FM groups, 35.6% vs 17.3%, and 51.2% vs 65.1%, respectively. NRM and OS were similar between groups, as well as time to ANC engraftment, aGHVD II-IV, and chronic GVHD (cGVHD). Platelet engraftment was 19 days versus 16 days for FB and FM, respectively (p=0.0023).
- Needing a dose adjustment based on AUC did not increase the risk for relapse or impact NRM.
- Despite busulfan pharmacokinetic monitoring, FB doubled the risk of relapse compared to FM. NRM and OS were similar between regimens. Further prospective, randomized studies should be conducted.

***Scott BL, Pasquini MC, Logan B et al. Results of a phase III randomized, multi-center study of allogeneic stem cell transplantation after high versus reduced intensity conditioning in patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML): blood and marrow transplant clinical trials network (BMT CTN) 0901. *Blood.* 2015;126(23):Abstr LBA-8.
https://ash.confex.com/ash/2015/webprogram/Paper87386.html

- The BMT CTN performed a phase III, multicenter, randomized trial comparing outcomes after myeloablative (MAC) versus RIC conditioning in 272 adult patients with MDS or AML. The planned enrollment was 356 patients; however, accrual was stopped early due to a presumed benefit of MAC as assessed by independent safety review.
- The primary outcome of the study, 18 month OS, was 77.4% MAC and 67.7% RIC (p=0.07) in the combined AML/MDS treatment groups. 18 month OS diverged when MDS and AML groups were stratified out by disease state, showing a statistically significant difference in survival in the AML disease group at 76.8% MAC and 63% RIC (p=0.027), with similar outcomes in the MDS group.
- A clinically significant difference was seen in relapse-free survival with 68.8% MAC and 47.3% RIC (p<0.01). TRM was 4.4% RIC versus 15.8% MAC (p=0.02), relapse on the RIC arm was 48.3% versus 13.5% on the MAC arm (p<0.01) and grade II-IV aGVHD was 31.6% RIC versus 44.7% MAC (p=0.024).
- This trial confirms that RIC results in higher relapse rates and lower TRM compared to MAC, with a statistically significant advantage in relapse-free survival for patients receiving MAC. MAC remains the treatment of choice over RIC, if the patient is an appropriate candidate for MAC.

**Richardson PG, Riches M, Kernan NA, et al. Defibrotide for the treatment of hepatic veno-occlusive disease/sinusodial obstruction syndrome with multi-organ dysfunction: final results from a pivotal, historically controlled, phase 3 trial. *Blood.* 2015;126(23):Abstr 737.
https://ash.confex.com/ash/2015/webprogram/Paper80232.html

- This trial was a historically controlled, multicenter, open-label, phase III study investigating the safety and efficacy of defibrotide (DF) versus historical controls (HC) in both adult and pediatric patients with established veno-occlusive disease/sinusoidal obstructive syndrome (VOD/SOS) and multiorgan dysfunction (MOD/MOF). There were 102 patients in the DF group and 32 cases selected as HCs.
- Survival at day +100 was 38% DF and 25% HC (p=0.0109). Observed CR rates at day +100 were 25.5% DF and 12.5% HC (p=0.016).
- The percentage of patients with adverse events (AEs) was similar across both treatment arms, with a comparable percentage of AEs leading to death. For the DF group, 45% had at least one AE potentially related to treatment with study drug, and 21% had at least one serious AE thought to be related to study drug. Hypotension was the most common AE in both groups.
- Based on the results of this analysis, DF provided a 23% improvement in survival and 19% improvement in CR rate at day +100, as compared to HC. AEs were consistent with those expected in this critically ill population and the overall incidence of hemorrhage and fatal AEs were similar between the two groups.

*Popat UR, Ray G, Bassett RL, et al. Eltrombopag for post-transplant thrombocytopenia: results of a phase II randomized double blind placebo controlled trial. *Blood.* 2015;126(23):Abstr 738.
https://ash.confex.com/ash/2015/webprogram/Paper83176.html

- A phase II, double blind, randomized, placebo controlled trial in 60 patients to investigate the safety and efficacy of eltrombopag for post-transplant thrombocytopenia.
- The primary endpoint was platelet count ≥ 30 x 10^9/L at the end of the 8 week treatment course. 36% of patients in the eltrombopag group achieved this goal, compared to 28% of patients in the placebo group, which did not meet the protocol specified probability, making the results inconclusive. For those patients that responded to therapy, response took at least 4 weeks.
- Transfusion requirements, OS, PFS, NRM and response rate were similar between groups. No significant difference in bone marrow fibrosis was seen between the two arms. There was no change in cataract rate, vision change or thrombosis among the two arms.
- Eltrombopag is safe, improves platelet count, and appears promising for post-transplant thrombocytopenia. The ideal dose and duration have yet to be defined and should be confirmed in future studies.

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

Literature updates composed and compiled by
Colleen Timlin, PharmD, BCOP