Literature summaries are provided as information only. Please refer to the original published articles for complete details on study methodology, results and discussion.

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


- Update of 2010 clinical practice guideline on CDI in adults by a panel of IDSA and SHEA experts. The update incorporates recommendations for children, includes significant changes in the management of CDI, and discusses the evolving controversy over best methods for diagnosis.
- For an initial CDI episode treatment, either vancomycin or fidaxomicin is recommended over metronidazole. Metronidazole PO for 10 days can be utilized for non-severe CDI only in settings where access to PO vancomycin or fidaxomicin is limited.
- For fulminant CDI (hypotension or shock, ileus, or megacolon), PO vancomycin is the regimen of choice in conjunction with IV metronidazole. If there is an ileus present, vancomycin administered rectally can be considered.
- Treat first recurrence of CDI with oral vancomycin as a tapered and pulse regimen or a 10-day course of fidaxomicin.


- Retrospective, observational study to investigate rates and outcomes of antibiotic de-escalation during pre-engraftment neutropenia in allo-HCT patients. The primary endpoint was the rate of early de-escalation. Secondary endpoints included rates of late de-escalation, de-escalation occurring at any time before engraftment, total days of antibiotic therapy saved by de-escalation, and outcomes (failure and survival at day +60).
- De-escalation was defined as narrowing the spectrum of antibiotic treatment either within (early) or after 96 hours (late) from antibiotic initiation. De-escalation failure was defined as restarting/escalating antibiotics within 96 hours after de-escalation.
- 102 patients were included in the analysis, 68 (67%) received monotherapy (predominantly piperacillin/tazobactam, n=58), and 34 (33%) received combination therapy (mainly meropenem plus glycopeptide, n=24). Median duration of neutropenia (granulocyte count <500 cells/mm³) was 17 days. Bloodstream infections were diagnosed in 28 patients (20%).
Early de-escalation rate was 25.5% (n=26) and mostly consisted of reducing the spectrum of beta-lactam antibiotics (42%, n=11). The failure rate of early de-escalation was 15% (4/26). Late de-escalation rate was 30.4% (n=31) and failure rate was 19% (6/31). The rate of de-escalation at any time before engraftment was 55.9% (n=57), including discontinuation in 33 patients (32%). The median saved antibiotic days were 10 for meropenem, 8 for piperacillin/tazobactam, and 7 for vancomycin. Death occurred in 3 patients before day +60 in patients that never underwent de-escalation.

The authors conclude that de-escalation, including discontinuation, is feasible and safe in pre-engraftment neutropenia after allo-HCT.


- Prospective, observational study in a single-center institution that included adult patients admitted for autologous or allogeneic HCT from April 2014 to September 2016 to determine if screening the GI tract to identify patients colonized with ESBL-E could identify recipients at high risk of developing ESBL-E bacteremia.
- All patients were treated with levofloxacin prophylaxis beginning on day -1.
- Ten percent of patients were colonized with ESBL-E prior to HCT. ESBL-E bacteremia only occurred in patients colonized with levofloxacin-resistant ESBL-E and all but one of the acquired ESBL-E were levofloxacin-resistant.
- In the setting of levofloxacin prophylaxis, 32% of colonized patients developed ESBL-E bacteremia during neutropenia post-HCT. The colonizing and bloodstream ESBL-E organisms were genetically identical.
- No significant differences in mortality rate were observed during the transplant admission (6% vs 2%, P=0.15), 100-day mortality rate (10% vs 7%, P=0.55), or the proportion of allogeneic HCT recipients who developed GVHD (47% vs 36%, P=0.30) in patients with and without pre-transplant ESBL-E colonization, respectively. There was no significant difference in time to administration of an antimicrobial agent to which the bloodstream isolate was susceptible in patients colonized and not colonized with ESBL-E.
- Findings have implications for antibacterial prophylaxis and empirical therapy at HCT centers where ESBL-E are prevalent bloodstream pathogens. In the setting of levofloxacin prophylaxis, screening the GI tract for colonization with levofloxacin-resistant ESBL-E identifies patients who are at high risk of developing ESBL-E bacteremia during their first episode of febrile neutropenia.

Hematopoietic Cell Transplantation


- Retrospective, single center analysis of 387 patients with myeloid or lymphoid hematologic malignancies undergoing 8/8 matched (related or unrelated) or 7/8 HLA-matched HCT with myeloablative conditioning using FluBu (fludarabine 30 mg/m² IV on days -5,-4,-3,-2 [120 mg/m² total] and busulfan 0.8 mg/kg IV every 6 hours for 16 doses on days -5,-4,-3,-2 without PK
monitoring) or CyTBI (cyclophosphamide 1800 mg/m$^2$ on days -6 and -5 and total body irradiation of 12 Gy or 14 Gy in twice-daily fractions).

- **Primary outcome was OS and secondary outcomes included PFS, NRM, aGVHD, and cGVHD.**
- **Patients received either FluBu (n=158) or CyTBI (n=229).** For the entire cohort, 3-year OS was similar (57% vs 55%; P=0.5). A multivariate analysis resulted in significantly improved 3-year OS for the FluBu group (65% vs. 55%; P=0.036). Relapse rates (HR 1.08; P=0.75) and cGVHD (HR 1.04; P=0.84) were similar between groups, but rates of NRM (HR 0.19; P=0.0003) and aGVHD (HR 0.45; P=0.0016) were worse with CyTBI.
- **The authors concluded that myeloablative conditioning with FluBu appears to be effective and more tolerable than CyTBI, leading to a better 3-year OS driven by improved NRM. Improvement in NRM was chiefly attributed to lower rates of grade II to IV aGVHD.**

- **Retrospective, single-center study to compare outcomes of auto-HSCT with melphalan conditioning in patients with MM between obese (>120% ideal body weight) and non-obese (<120% ideal body weight) populations.**
- **Primary outcome was 3-year EFS and was assessed by a noninferiority design with a pre-determined noninferiority margin of 7%.** Secondary outcomes assessed included response at 100 days post-transplantation, 3-year OS, TRM, time to neutrophil engraftment, and hospital length of stay.
- **270 patients, including 171 (63%) obese and 99 (37%) non-obese were enrolled in the study.** Baseline characteristics were well matched, including high-risk cytogenetics, disease severity at diagnosis, and use of maintenance therapy post-transplant.
- **The 3-year EFS for the entire study population was 41%, with significantly less events in the obese cohort (51% vs. 40%; P=0.0025).** The 95% lower confidence limit established this as noninferior. There were no between-group differences in TRM, time to engraftment, or hospital length of stay.
- **The authors conclude that using adjusted body weight melphalan dosing in obese patients is not inferior to non-obese populations in terms of 3-year event-free survival.**

- **Retrospective review of 577 patients with MM who underwent early auto HCT between 2010 and 2015 after IMiD based induction therapy at the Mayo Clinic.**
- **132 patients received Len maintenance, 104 received Bort maintenance and 341 received no maintenance.**
- **Patients receiving Len had higher risk cytoge necics and were less likely to have achieved a CR or sCR by day +100 compared to no maintenance; similarly patients receiving Bort maintenance had higher risk cytogenics but were younger than the no maintenance group.**
- **Len maintenance improved PFS in all subgroups regardless of cytogenetic or ISS staging compared to no maintenance; 36.5 vs 27.7 months (p < 0.002).** OS was similar between groups.
- **Bort maintenance did not improve PFS in the entire cohort compared to no maintenance; 26.4 vs 27.7 months (p = 0.556).** OS rates at 4-years appeared lower in the Bor group; 64% vs 80% (p=0.004) however the negative impact of Bort did not persist on multivariate analysis.
• Patients with high-risk cytogenetics in the Bort group did have superior PFS compared to no maintenance; 28 vs 16 months (p = 0.035).
• More patients in the Len group remained on therapy at the last follow up than Bort (33% vs 26%) however Bort was associated with lower discontinuation due to toxicity (17% vs 6%). Secondary malignancies were reported in 4.6% with Len, 2% with Bort, and 5% with no maintenance.
• Real-world data regarding effects of Len and Bort maintenance therapy. Although the Bort did not appear to impact PFS, there was inherent selection bias of high-risk patients to Bort which may have impacted this outcome. Receiving Bort did seem to abrogate the negative risk factors of these high-risk patients. Ultimately, the data confirms previous studies regarding benefit of IMID maintenance and suggests Bort may be an alternative in high-risk patients were toxicity or financial burden may be a concern.


• Transplant related review from the “Update on Hodgkin lymphoma” review series in Blood
• Reviews pre-transplant treatment options, PET imaging status, salvage therapies, conditioning regimens, therapies for relapse post-transplant, and consideration of allogeneic transplant
• Recommendations include:
  o PET negativity pre-transplant is preferred but positive PET should not exclude patients from proceed to auto HCT.
  o No single salvage regimen pre-transplant is preferred and choice should be patient-specific; sequential therapy with BV to combination chemo recommended with up to 2 salvage programs pre-auto HCT.
  o BEAM remains standard conditioning regimen but could consider CBV.
  o BV is preferred therapy for relapse post auto. Checkpoint inhibitors could be considered as well. Regardless of initial choice, patients should be reviewed for allo-HCT eligibility.

**Mobilization**

• Prospective evaluation of the impact of DMSO concentration on engraftment after auto HCT.
• Patients (n=155) were randomly assigned to 10%, 7.5% or 5% DMSO cryopreservation in their leukapheresis products. The study groups did not differ based on diagnosis (mainly lymphoma and multiple myeloma), age, conditioning regimen, and the number of transplanted hematopoietic stem cells.
• The frequency of adverse effects during and shortly after infusion was the lowest in 5% DMSO arm (p = 0.02 compared to 10% DMSO). The median time to leukocyte and neutrophil recovery was 10 days in all study groups (p = 0.36 and p = 0.2). Median day of platelet recovery was the same for all DMSO concentrations and equaled 15 days (p = 0.61).
• The authors conclude, 5% DMSO mixture may be considered a new standard in cryopreservation of hematopoietic stem cells.


- Retrospective evaluation of stem cell mobilization in 610 patients with light chain amyloidosis, of which 79 had prior exposure to melphalan, 167 to other chemotherapeutics, and 364 had no chemotherapy exposure.
- Median total yields (stem cells x 10^6/kg) in the melphalan, non-melphalan, and no chemotherapy groups were 5.5, 7.7, and 7.8, respectively; p < 0.001. Day 1 yields were 2.7, 3.5, and 4 (p = 0.0003), respectively, and median yields per collection were 2, 3.3, and 4 (p < 0.001), respectively.
- Similar results were observed in the sub-group analysis after plerixafor was integrated into the algorithm.
- Patients in the melphalan group had higher failure rates of 9% vs. 2% each in the other two groups (p = 0.006).
- The impact of melphalan appears dose-dependent with cumulative melphalan exposure of >150 mg (median: three cycles) resulting in lower yields. The authors suggest that the duration of melphalan exposure prior to stem cell collection should be limited to no more than two cycles of treatment.

**Graft-versus-Host Disease**
*van der Wagen L, te Boome L, Schiffler M, et al. Prospective evaluation of sequential treatment of sclerotic chronic graft versus host disease with rituximab and nilotinib. *Bone Marrow Transplant.* 2018; [Epub ahead of print].


- The first prospective phase II trial to evaluate whether sequential therapy of rituximab followed by 6 months of treatment with nilotinib is a favorable treatment strategy for sclerotic cGVHD.
- Adult patients (n = 29) were eligible with cGVHD and skin localization refractory to or dependent on first-line treatment with steroids and/or calcineurin inhibitors. The treatment consisted of rituximab 375 mg/m² IV weekly for 4 doses followed by nilotinib 300 mg oral twice a day initiated the following week.
- Objective responses occurred in 71% of patients (two patients CR, 15 patients PR). Moreover, two out of five patients suffering from severe ulcerations showed complete resolution of ulcers. The majority of responding patients could reduce daily corticosteroid dose with more than 50%.
- The authors conclude that sequential treatment of rituximab followed by nilotinib is associated with a very high response rate in this difficult to treat patient population.

**Pediatrics**


- Comprehensive review of early and late musculoskeletal complications following TBI in hematopoietic stem cell transplant patients.
- The review highlights certain late effects from TBI such as short stature, osteonecrosis, slipped capital femoral epiphysis, and the development of benign and malignant bone tumors.
With a growing number of childhood cancer survivors, there is a need for greater awareness of these complications in order to ensure prompt treatment and improved outcomes for survivors.

**Other**


- Retrospective, matched cohort evaluation to study the safety and efficacy of ECP for BOS, where patients with BOS receiving ECP where compared to non-ECP patients. Endpoints assessed were overall survival, FEV₁ percentage predicted (FEV₁pp), patients receiving >5 mg prednisone daily, and decline in Karnofsky performance score.
- 26 patients with a diagnosis of BOS (median transplant age of 50 years) received ≥3 months of ECP and were included in the study. 26 patients were included as their matched pair via propensity-score matching for BOS severity. The rate of decline in FEV₁pp after ECP initiation was not significantly different between groups (P=0.33). At last follow-up, non-ECP patients were more likely to be on >5 mg of prednisone daily (54% vs. 23%; P=0.04) and had a greater decline in their Karnofsky performance score (mean difference -9.5 vs. -1.6; P=0.06).
- On multivariate analysis, MRD HCT (HR 0.1 [0.03-0.5]; P=0.002), ECP (HR 0.1 [0.01-0.3]; P=0.001), and slower rate of decline in FEV₁pp before ECP/index date (HR 0.7 [0.6-0.8]; P=0.001) were associated with a better overall survival.
- The authors conclude that, in patients with BOS, ECP may improve overall survival without significantly impacting measured pulmonary function.

**Abbreviations**

aGVHD: acute graft versus host disease  
Allo-HCT: allogeneic hematopoietic stem cell transplant  
Auto-HCT: autologous hematopoietic stem cell transplant  
Bort: bortezomib  
BOS: bronchiolitis obliterans syndrome  
BV: brentuximab vedotin  
CDI: *Clostridium difficile* infection  
cGVHD: chronic graft versus host disease  
CR: complete response  
DMSO: Dimethyl sulfoxide  
ECP: extracorporeal photopheresis  
EFS: event-free survival  
ESBL-E: extended-spectrum β-lactamase-producing Enterobacteriaceae  
GI: gastrointestinal  
GVHD: graft-versus-host disease  
HCT: hematopoietic cell transplantation  
IV: intravenous  
Len: lenalidomide  
MM: multiple myeloma  
MRD: matched related donor  
NRM: non-relapse mortality
OS: overall survival
PET: positron emission tomography
PFS: progression-free survival
PJP: *Pneumocystis jirovecii* pneumonia
PO: by mouth
PR: partial response
TBI: total body irradiation
TSQM: Treatment Satisfaction Questionnaire for Medication

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