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

Hematopoietic Cell Transplantation

*Dodero A, Patriarca F, Milone G, et al. Allogeneic stem cell transplantation for relapsed/refractory B cell lymphomas: results of a multicenter phase II prospective trial including rituximab in the reduced-intensity conditioning regimen. *Biol Blood Marrow Transplant*. 2017; 23:1102-9. https://www.ncbi.nlm.nih.gov/pubmed/28390983

- Multicenter phase II prospective trial to assess the effect on disease outcomes and rates of aGVHD and cGVHD of one dose of rituximab in the RIC regimen for adult patients undergoing allogeneic HCT for relapsed/refractory, CD20+ B-cell lymphomas (n=121).
- Conditioning consisted of thiotepa, cyclophosphamide, fludarabine, and rituximab (500 mg/m^2); rabbit ATG was given for unrelated donors. There were 55% of patients who received related grafts and 45% unrelated.
- At a median follow up of 41 months, the primary endpoint of 3-year PFS was 50%. This did not demonstrate improvement compared to historical data without rituximab. The 3-year TRM was 20%; NRM was 21%, OS was 61% and relapse was 25%; at 3 years, 54% of patients with previous auto and 43% of patients not in CR were alive
- Study utilized a novel composite endpoint, GRFS, to assess long-term outcomes with 1-year and 3-year GRFS of 40% and 34%, respectively.
- Authors concluded that allogeneic HCT may provide cure in a fraction of patients with relatively low rates of NRM and encouraging PFS and GRFS. The utility of including rituximab in the preparative regimen remains to be determined, as this study was closed early due to slow accrual and the availability of other trials investigating novel agents and use of haploidentical donors.

*Yanada M, Mori J, Aoki J, et al. Effect of cytogenetic risk status on outcomes for patients with acute myeloid leukemia undergoing various types of allogeneic hematopoietic cell transplantation: an analysis of 7812 patients. *Leukemia & Lymphoma*. 2017 July 28. [Epub ahead of print] DOI: 10.1080/10428194.2017.1357173. https://www.ncbi.nlm.nih.gov/pubmed/28750566

- This is a retrospective registry to determine how cytogenetic risk status affects outcomes for patients with AML post allo-HCT.
- Of 7812 Japanese patients eligible for analysis between 2002 and 2012, cytogenetic risk was classified as favorable for 1088, intermediate for 5025, and poor for 1699.
- Patients with favorable cytogenetics showed significantly lower risks of relapse (HR, 0.87; 95% CI, 0.77–0.99; p = 0.035) and overall mortality (HR, 0.90; 95% CI, 0.81–0.99; p = 0.036), while patients with poor cytogenetics showed significantly higher risks of relapse (HR, 1.54; 95% CI, 1.41–1.68; p < .001) and overall mortality (HR, 1.42; 95% CI, 1.38–1.58; p < .001) both compared

to intermediate-risk groups. NRM was identical for the three groups (HR, 0.97; 95% CI, 0.84–1.12; p = 0.711 for favorable vs intermediate; and HR, 0.93; 95% CI, 0.82–1.04; p = 0.205 for poor vs intermediate).

- Multivariate analysis showed significant differences in relapse and survival between groups, with the difference between poor- and intermediate-risk groups being greater than that between favorable- and intermediate-risk groups. The authors conclude this study confirms that cytogenetic risk status strongly affects survival post allo-HCT in patients with AML.

*Tandon N, Muchtar E, Sidana S, et al. Revisiting conditioning dose in newly diagnosed light chain amyloidosis undergoing frontline autologous stem cell transplant: impact on response and survival. *Bone Marrow Transplant*. 2017;52(8):1126-32. https://www.ncbi.nlm.nih.gov/pubmed/28394369

- Retrospective, single-center study comparing full-dose melphalan conditioning (n=314) vs reduced-dose melphalan conditioning (n=143) in ASCT patients with light chain amyloidosis.
- Patients in the full-intensity group were younger, had a higher proportion with Karnofsky performance score of 80 or greater, had lower plasma cell tumor burden, less multiorgan and cardiac involvement and had a higher percentage of patients in lower Mayo stages as compared with patients in the reduced-intensity group.
- Full-dose conditioning (200mg/m^2) was associated with higher rate of VGPR or better (79% vs 62%; p<0.001), CR rate (53% vs 37%; p=0.003) and organ response rate (74% vs 59%; p=0.002) as compared to reduced-dose conditioning (<180mg/m^2).
- PFS was superior in the full-intensity group compared to the reduced-dose group (4-year PFS 55% vs 31%; p<0.001) as well as 4-year OS (86% vs 54%; p<0.001).

*Kwon M, Bautista G, Balsalobre P, et al. Haplo-cord transplantation compared to haploidentical transplantation with post-transplant cyclophosphamide in patients with AML. *Bone Marrow Transplant*. 2017;52(8): 1138-43. https://www.ncbi.nlm.nih.gov/pubmed/28346415

- Retrospective study comparing umbilical cord blood transplant supported by a third-party HLA-mismatched donor (n=51) vs haploidentical transplant with PTCy (n=36) in AML patients.
- Incidence of grades II-IV acute GVHD at day +180 in PTCy-haplo group was 29% vs 9% in cord-blood group. (p=0.02) Incidence of cGVHD was 38% in PTCy-haplo group vs 20% in the haplo-cord group. (p=0.03).
- With a median follow-up of 61 months for the haplo-cord group and 26 months for the PTCy–haplo cohort, OS at 2 years was 55% and 59% (p=0.66), EFS was 45% vs 56% (p=0.46), relapse rate was 27% vs 21% (p=0.79), and NRM was 17% vs 23% (p=0.54), respectively. Cumulative incidence of neutrophil engraftment was 97% in the haplo-cord and 100% in the PTCy–haplo group, achieved in a median of 12 and 17 days, respectively (p=0.01).
- The authors concluded that both haplo-cord and PTCy-haplo HCT are both valid donor alternatives for patients with AML.
- The authors concluded that this study demonstrated that amyloidosis patients treated with ASCT in first line have inferior response and shorter survival with the use of reduced-dose melphalan even after taking factors leading to dose reduction into account.

*Martino R, Henseler A, van Lint M, et al. Long-term follow-up of a retrospective comparison of reduced-intensity conditioning and conventional high-dose conditioning for allogeneic transplantation from matched related donors in myelodysplastic syndromes. *Bone Marrow Transplant*. 2017;52(8):1107-12. https://www.ncbi.nlm.nih.gov/pubmed/28319072

- International, retrospective study that analyzed long-term follow-up of 843 patients with MDS that underwent an allogeneic transplant after either a RIC or MAC regimen at a median long-term follow-up of 13 years.
- 13-year relapse rate was significantly increased after RIC (31% in MAC vs 48% in RIC, p=0.04). OS (30% in MAC, 27% in RIC) and PFS (29% in MAC, 21% in RIC) showed no difference.
- NRM had an increased trend in all MAC patients, but was significantly higher in MAC patients older than 50 years (50% vs 33%, p <0.01).
- Long-term follow-up in this 13-year study confirms other variables with significant impact on outcomes include MDS risk category, disease phase at time of transplant, cytogenetic profile, and higher donor cell dose.

Pediatrics

*Locatelli F, Merli P, Pagliara D, et al. Outcome of children with acute leukemia given HLA-haploidentical HSCT after αβ T-cell and B-cell depletion. *Blood*. 2017;130(5):677-685. https://www.ncbi.nlm.nih.gov/pubmed/28588018

- A novel method of graft manipulation based on a selective depletion of αβ T and B-cell haploidentical HCT in children with acute leukemia was used and outcomes were evaluated.
- 80 children, transplanted between September 2011 and September 2014, were enrolled in this prospective, single-center, phase II trial. All children were given a fully myeloablative preparative regimen. Anti–T-lymphocyte globulin from day -5 to -3 was used for preventing graft rejection and GVHD; no patient received any post-transplantation GVHD prophylaxis. This group was compared to 41 and 51 patients transplanted in the same time period and center for either a HLA-identical sibling or a 10/10 MUD, respectively.
- Median follow up was 46 months for surviving patients, and the 5-year chronic GRFS was 71%. A TBI–containing preparative regimen was the only favorable variable to impact relapse incidence and GRFS.
- The outcomes of these 80 patients are similar to the comparator group. The authors conclude this is a competitive alternative for children with acute leukemia in need of urgent allograft.

*Heimall J, Buckley RH, Puck J, et al. Recommendations for screening and management of late effects in patients with severe combined immunodeficiency after allogeneic hematopoietic cell transplantation: A consensus statement from the second Pediatric Blood and Marrow Transplant Consortium International Conference on Late Effects after Pediatric HCT. *Biol Blood Marrow Transplant*. 2017;23:1229-40. https://www.ncbi.nlm.nih.gov/pubmed/28479164

- International panel provided recommendations for screening and management of late effects associated with transplant in pediatric and adult SCID patients.
- Recommendations regarding immune function and infection risk, non-immune organ system late effects, and genetic counseling are included, as well as a sample document to assist with long-term monitoring of patients.
- Provides specific recommendations around immune function support with vaccinations, IVIG supplementation and immune reconstitution monitoring. Specific recommendations are provided for a variety of long term effects including thyroid dysfunction, psychosocial support, pulmonary dysfunction, gonadal function, endocrine function, etc.

Other

*Bug G, Burchert A, Wagner EM, et al. Phase I/II study of the deacetylase inhibitor panobinostat after allogeneic stem cell transplantation in patients with high-risk MDS or AML (PANOBEST Trial). *Leukemia*. 2017 July 28. [Epub ahead of print] DOI: 10.1038/leu.2017.242. https://www.ncbi.nlm.nih.gov/pubmed/28751769

- Open label, multi-center phase I/II trial assessing the feasibility and preliminary efficacy of maintenance panobinostat post-HCT for AML or MDS.
- 42 patients (37 AML, 5 MDS) were included between January 2011 and January 2015. Enrollment occurred at a median of 96 days post-HCT. Patients were required to be in CR post-HCT and fulfill one or more of the following criteria: (i) AML refractory or with delayed response to or relapsed after ≥ one cycle of standard chemotherapy; (ii) adverse risk cytogenetics (iii); secondary to MDS or radio-/chemotherapy, iv) MDS intermediate-2 or high-risk according to IPSS or MDS RAEB (WHO classification).
- Patients received panobinostat at a dose of either 20 mg TIW every week or 30 mg TIW every other week.
- 83% of patients experienced at least one grade 3/4 adverse event, and 52% were considered panobinostat-related. 2-year OS and RFS are 81% (95% CI, 69-95%) and 75% (95% CI, 63-90%), respectively.
- The authors conclude that the alternate week dosing regimen was better tolerated, and the outcomes in their high-risk AML/MDS population compares favorably with survival and cumulative relapse rates reported for similar patient cohorts. Further study on the role of panobinostat maintenance will be conducted in a large European randomized trial.

**Goldschmidt H, Lokhorst HM, Mai EK, et al. Bortezomib before and after high-dose therapy in myeloma: long-term results from the phase III HOVON-65/GMMG-HD4 trial. *Leukemia*. 2017 August 1. [Epub ahead of print] DOI: 10.1038/leu.2017.211. https://www.ncbi.nlm.nih.gov/pubmed/28761118

- Phase III multicenter trial with the Dutch-Belgian Cooperative Trial Group for Hematology Oncology Group-65/German-speaking Myeloma Multicenter Group HD4 (HOVON-65/GMMG-HD4) utilizing bortezomib before and after high-dose melphalan and auto-HCT (PAD arm) compared with classical cytotoxic agents prior and thalidomide after auto-HCT (VAD arm) in multiple myeloma patients aged 18–65 years.
- The primary endpoint was PFS. There was also a long term follow up analysis on SPMs.
- With a median follow-up of 96 months, PFS was significantly prolonged in the PAD versus VAD arm (hazard ratio = 0.76, 95% CI of 0.65–0.89, P = 0.001). OS was similar in the PAD versus VAD arm (HR = 0.89, 95% CI: 0.74–1.08, P = 0.24). The incidence of SPMs were similar between the two arms (7% each, P = 0.73).
- The authors concluded the PFS benefit with bortezomib induction and maintenance compared with classical cytotoxic agents and thalidomide maintenance is sustained without an increased risk of SPM, and is considered a standard of care option.

Abbreviations
ASCT: autologous stem cell transplant
AML: acute myeloid leukemia
CR: complete response
EFS: event-free survival
GRFS: GVHD-free, relapse-free survival
GVHD: graft-versus-host disease
HCT: hematopoietic cell transplantation
HLA: human leukocyte antigen
IPSS: International Prognostic Scoring System
MAC: myeloablative conditioning
MDS: myelodysplastic syndrome
NRM: non-relapse mortality
OS: overall survival
PFS: progression-free survival
PTCy: post-transplant cyclophosphamide
RAEB: refractory anemia with excess blasts
RFS: relapse-free survival
RIC: reduced intensity conditioning
SCID: severe combined immunodeficiency syndrome
SPM: second primary malignancy
TBI: total body irradiation
TRM: transplant-related mortality
TIW: thrice weekly
VGPR: very good partial response

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