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

**Muffly L, Pasquini MC, Martens M, et al. Increasing use of allogeneic hematopoietic cell transplantation in patients aged 70 years and older in the United States. *Blood*. 2017;130(9):1156-64. https://www.ncbi.nlm.nih.gov/pubmed/28674027

- Retrospective review of trends and outcomes in patients ≥70 years old reported to CIBMTR with a hematologic malignancy undergoing first allo-HCT in the US between 2000 and 2013
- 1106 patients were included across 103 transplant centers. AML and MDS were the most common disease indications.
- Over time, 2-year OS and PFS significantly improved, OS: 26% in 2000-2007 to 39% in 2008-2013 ($p<0.001$); PFS: 22% in 2000-2007 to 32% in 2008-2013 ($p=0.003$). Two-year TRM was 33% to 35% and was not different between time groups ($p=0.54$). Multivariable analysis of OS in the 2008-2013 group revealed higher comorbidity, with adverse factors of HCT comorbidity index ≥3 (HR, 1.27; $p=0.006$), umbilical cord blood graft (HR, 1.97; $p=0.0002$), and myeloablative conditioning (HR, 1.61; $p=0.0002$).
- The authors conclude that the survival has increased over time in this population and transplant should be considered in select patients ≥70 years old with a hematologic malignancy.

*Anguille S, Van de Velde AL, Smits EL, et al. Dendritic cell vaccination as post-remission treatment to prevent or delay relapse in acute myeloid leukemia. *Blood*. 2017 August 22. [Epub ahead of print] doi: 10.1182/blood-2017-04-780155. https://www.ncbi.nlm.nih.gov/pubmed/28830889

- Phase II study in 30 AML patients in remission but at very high risk of relapse, evaluating the outcomes of vaccination with dendritic cells electroporated with WT1 mRNA as post-remission adjuvant therapy.
- There was a demonstrable anti-leukemic response in 43% of patients (n=13). Nine of these achieved molecular remission and 5 have sustained after a median follow-up of 109.4 months.
- Five-year OS was significantly higher in responders than in non-responders (53.8% vs. 25.0%; P=0.01). Long-term clinical response was correlated with WT1-reactive CD8+ T-cell immunity induced by the DC vaccine.
- The authors conclude that DC vaccination can promote anti-leukemic T-cell immunity, providing a non-toxic, adjuvant therapy to decrease the risk of relapse and improve OS in very high risk AML patients.

*Rosinol L, Oriol A, Teruel AI, et al. Bortezomib and thalidomide maintenance after stem cell transplantation for multiple myeloma: a PETHEMA/GEM trial. *Leukemia*. 2017 Sep;31(9):1922-1927. https://www.ncbi.nlm.nih.gov/pubmed/28111466

- Randomized phase III trial of the Spanish Myeloma Group (PETHEMA/GEM) comparing induction with TD vs. VTD vs. VBMCP/VBAD/B in patients ≤ 65 years old with newly diagnosed symptomatic MM and auto-HCT with melphalan 200 mg/m^2, followed by maintenance with thalidomide/bortezomib (TV) vs. thalidomide (T) vs. alfa-2b interferon (alfa2-IFN). This study is reporting the results of the maintenance portion.
- Maintenance treatment consisted of thalidomide 100 mg daily plus intravenous bortezomib at 1.3 mg/m^2 on days 1, 4, 8 and 11 every 3 months (TV arm) versus thalidomide 100 mg daily (T arm) versus alfa2-IFN 3 MU three times per week (alfa2-IFN arm) for up to 3 years.
- There were 271 patients randomized (TV: 91; T: 88; alfa2-IFN: 92). Comparing maintenance regimens, CR was improved by 21% with TV, 11% with T and 17% with alfa2-IFN (P, NS). Additionally, PFS was significantly longer with TV compared with T and alfa2-IFN (50.6 vs 40.3 vs 32.5 months, P = 0.03) after a median follow-up of 58.6 months. CR in TV patients was significantly greater than T patient (p=0.04), but was no different than patients receiving alpha2-IFN (p=0.5). OS was not significantly different. Grade 2–3 peripheral neuropathy was reported in 48.8%, 34.4% and 1% of patients treated with TV, T and alfa2-IFN, respectively.
- The authors conclude maintenance therapy with TV resulted in significantly longer PFS when compared with thalidomide or alfa2-IFN.

**Esquirol A, Pascual MJ, Ortiz M, et al. Single-agent GvHD prophylaxis with tacrolimus after post-transplant high-dose cyclophosphamide is a valid option for haploidentical transplantation in adults with hematologic malignancies. *Bone Marrow Transplant*. 2017;52(9):1273-79. https://www.ncbi.nlm.nih.gov/pubmed/28604667

- 81 patients with high-risk hematological malignancies received an unmanipulated haploidentical stem cell transplant with a thiotepa/busulfan/fludarabine conditioning regimen at four different Spanish institutions.
- GVHD prophylaxis consisted of high-dose cyclophosphamide on days +3 and +4 and single-agent IV tacrolimus starting on day +5 with goal levels of 5-10 mcg/L and progressively discontinuing dose after 7 months of therapy.
- Median time to neutrophil and platelet count recovery were 18 and 23 days, respectively, and 93% of patients achieved full donor chimerism by day +30. 1-year OS and PFS were 61% and 51%, respectively. Cumulative incidence of NRM and relapse at 1-year were also 27% and 19%, respectively.
- Cumulative incidence of grades II-IV and III-IV acute GvHD were 23% and 14%, respectively. For chronic GvHD, the cumulative incidence of limited stage was 20% and extensive stage was 22%.
- The authors concluded that patients with hematological malignancies undergoing haploidentical stem cell transplant may benefit from less pharmacological prophylaxis for GVHD, but graft-versus-tumor effect and effect on relapse requires further investigation.

*Kassam S, Chernucha E, O'Neill A, et al. High-dose chemotherapy and autologous stem cell transplantation for primary central nervous system lymphoma: a multi-centre retrospective analysis from the United Kingdom. *Bone Marrow Transplant*. 2017;52(9):1268-72. https://www.ncbi.nlm.nih.gov/pubmed/28581466

- Multicenter, retrospective study of 70 patients with primary central nervous system lymphoma who underwent induction with high-dose methotrexate containing regimens followed by thiotepa-based HDC-ASCT in first response.
- CR rate increased from 50% before HDC-ASCT consolidation to 77% after HDC-ASCT consolidation. TRM in the HDC-ASCT consolidation group was 6%. At a median follow-up of 12 months from HDC-ASCT, the estimated 1- and 2-year PFS rates were 71.5% and OS rates were 86.4% and 83.3%, respectively.
- The authors report that these results are comparable to previous literature and that most patients were able to avoid whole-brain radiation therapy, which is a potential cause of neurocognitive dysfunction.

Graft-versus-Host Disease

**Malard F, Labopin M, Yakoub-Agha I, et al. Rituximab-based first line treatment for chronic GVHD after allogeneic SCT: results of a phase 2 study. *Blood*. 2017 Sept 1. [Epub ahead of print] doi: 10.1182/blood-2017-05-786137 https://www.ncbi.nlm.nih.gov/pubmed/28864814

- Phase II, prospective, multicenter trial to evaluate the efficacy of the addition of rituximab to corticosteroid 1 mg/kg/day and cyclosporine A as first line therapy for newly diagnosed chronic GVHD requiring systemic therapy
- 24 patients (median age, 47 years) with mild (n=2), moderate (n=7) or severe (n=15) chronic GVHD were included. Patients received rituximab 375 mg/m^2 weekly for 4 weeks; those achieving PR received a second course one month later.
- ORR was 83% (n=20) at 1-year after rituximab administration. The estimated 1-year OS was 83% and the 1-year cumulative incidence of NRM was 14%.
- The authors conclude the addition of rituximab to corticosteroid and cyclosporine A appeared to be safe and effective for first line treatment of cGVHD.

Other

* Radujkovic A, Kordelas L, Krzykalla J, et al. Pretransplant vitamin D deficiency is associated with higher relapse rates in patients allografted for myeloid malignancies. *J Clin Oncol*. 2017; 35:3143-52. https://www.ncbi.nlm.nih.gov/pubmed/28771378

- Retrospective, cohort study to assess the pre-transplant vitamin D status in patients undergoing allo-HCT from 2002 to 2013. Cohort one (training cohort) consisted of 492 patients allografted for myeloid and lymphoid malignancies between 2002 and 2013. Cohort two (validation cohort) consisted of 396 patients diagnosed with AML or MDS who underwent transplant between 2009 and 2013.
- In the training cohort, the median pre-transplant 25-hydroxy vitamin D (25D3) serum level was 11.8 ng/mL (range, 4-46.3 ng/mL) and a total of 396 patients (80%) were vitamin D deficient pre-transplant (defined as 25D3 < 20 ng/mL). The validation cohort had a median pre-transplant 25D3 level of 10.5 ng/mL (range, 4-39.2 ng/mL) with 348 patients (87%) vitamin D deficient before transplant.

- In multivariate analysis of the training cohort, pre-transplant vitamin D deficiency was associated with significantly higher risk of relapse (HR, 1.96; P = 0.006) and inferior survival (HR, 1.78; P = 0.007). There was also a trend toward higher risk of NRM (HR, 1.72; P = 0.088).
- Pre-transplant vitamin D deficiency was associated with a significantly higher risk of relapse in patients with myeloid malignancies (HR, 2.55; P = 0.014), but not in patients with lymphoid malignancies (HR, 1.60; P = 0.147). A similar impact of pre-transplant vitamin D deficiency on relapse risk in patients with myeloid diseases was also observed in the validation cohort (HR, 2.60; P = 0.017).
- In patients undergoing allo-HCT for myeloid malignancies, pre-transplant vitamin D deficiency was associated with a significantly higher risk of relapse, indicating the need for prospective studies evaluating vitamin D status and correction of vitamin D deficiency in the setting of HCT.

Abbreviations

Allo-HCT: allogeneic hematopoietic stem cell transplant
AML: acute myeloid leukemia
Auto-HCT: autologous hematopoietic stem cell transplant
cGVHD: chronic graft-versus-host disease
CIBMTR: Center for International Blood and Marrow Transplant Research
CR: complete response
DC: dendritic cells
GVHD: graft-versus-host disease
HCT: hematopoietic stem cell transplant
HDC-ASCT: high-dose chemotherapy and autologous stem cell transplant
MDS: myelodysplastic syndrome
MM: multiple myeloma
NRM: non-relapse mortality
NS: not significant
ORR: overall response rate
OS: overall survival
PFS: progression-free survival
PR: partial response
TD: thalidomide/dexamethasone
TRM: transplant-related mortality
VBMCP/VBAD/B: vincristine, BCNU, doxorubicin, dexamethasone/bortezomib
VTD: bortezomib/thalidomide/dexamethasone
WT: wild type

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