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


- Randomized, multicenter phase III trial comparing MAC (n=135) versus RIC (n=137) followed by HCT from MRD or MUD in adult patients with AML or MDS.
- Accrual ended early due to significantly higher relapse at 18 months with RIC (48.3%; 95% CI, 39.6% to 56.4%) versus MAC (13.5%; 95% CI, 8.3% to 19.8%) (P<.001); relapse was the primary cause of death (86.4%) for those receiving RIC.
- TRM at 18 months was significantly higher in the MAC arm (15.8%; 95% CI, 10.2% to 22.5%) versus the RIC arm (4.4%; 95% CI, 1.8% to 8.9%) (P=.002); GVHD was the primary cause of death (50%) for those receiving MAC.
- The primary endpoint of OS at 18 months post-random assignment was 77.5% (95% CI, 69.4% to 83.7%) in the MAC arm and 67.7% (95% CI, 59.1% to 74.9%) in the RIC arm (P=.07); this was not statistically significant.
- When treating death and relapse as competing risks, the cumulative incidence of grade 2-4 GVHD at day 100 was 44.7% (95% CI, 36% to 53%) with MAC and 28.6% (95% CI, 21% to 36%) with RIC (P=.006); grade 3-4 GVHD at day 100 was 14.4% (95% CI, 9% to 21%) with MAC and 3.8% (95% CI, 1% to 8%) with RIC (P=.003); chronic GVHD at 18 months was 65.6% (95% CI, 57% to 73%) with MAC and 36.9% (95% CI, 28% to 45%) with RIC (P<.01).
- The authors concluded that although RIC lowered TRM, this benefit was offset by significantly higher relapse rates in those receiving MAC. Even though the difference in OS was not statistically significant, OS was numerically lower for those receiving RIC. The data supports the use of MAC as standard of care for fit patients with AML or MDS.


- Prospective, non-randomized study of 15 heavily-transfused patients with BMFS who underwent MRD HCT with GCSF-mobilized T-cell depleted CD34+ cells co-infused with a BMT equivalent dose of non-mobilized donor T-cells. Outcomes were compared with a historical cohort of 56 similar patients who received unmanipulated PBSC transplant.
All patients in the study cohort achieved neutrophil recovery occurring at a median time of 14 days (range 10-23), 14/15 (93%) achieved platelet recovery at a median time of 18 days (range 9-321), and none experienced graft rejection. Results were similar in both cohorts.

All patients in the study cohort achieved full donor (≥95%) T-cell and myeloid chimerisms at a median time of 30 days (range 15-730) and 15 days (range 15-30) post-transplant, respectively. Although myeloid engraftment was similar to the historical cohort, the study cohort was significantly slower in achieving full-donor T-cell chimerism (53% vs 82% by day 30; P=0.014).

Two patients each (13%) developed acute grade II-IV (95% CI: 2-35) and chronic GVHD (95% CI: 2-35) in the study cohort at day 100. The historical cohort experienced significantly more grade II-IV acute GVHD (13% vs 52%; P=0.010) and chronic GVHD (13% vs 72%; P=0.0004).

With a median follow-up of 42 months (range 11-61), 13 out of 15 patients in the study cohort survived, for an estimated OS probability of 86% (95% CI: 71-100). OS was comparable between cohorts (86% vs 87%; P=0.86).

Although this method showed delayed T-cell reconstitution, the authors concluded that this method achieves excellent engraftment and survival with a reduction in acute and chronic GVHD without increasing the risk of graft rejection. These findings are hypothesis-generating and warrant further investigation especially among lower-risk SAA patients with treatment-naïve disease.


Twenty-five patients with AML and 6 patients with MDS were treated with a fludarabine 150 mg/m² and treosulfan 42 g/m² (FluTreo) regimen (plus anti-thymocyte globulin 5 mg/kg for unrelated donors) compared with 26 historical controls treated with a fludarabine 150-180 mg/m², busulfan 6.4 mg/kg, anti-thymocyte globulin 5-7.5 mg/kg ( FluBuATG) regimen. Of note, there were more MUD recipients in the FluTreo group (p<0.001).

No grade III or grade IV organ toxicities were observed in either group. 1-year OS probability was 76% with FluTreo and 57% in FluBuATG (p=0.026) and DFS was 79% vs 38% (p<0.001). In multivariate analysis, the only significant favorable factor for OS and DFS was use of the FluTreo regimen (p=0.010, p=0.012).

Relapsed mortality at 1 year was significantly lower in the FluTreo group compared to the FluBuATG group (7.4% vs 42.3%, P<0.001).

Rates of acute and chronic GVHD (P=0.426 and 0.247, respectively) and TRM (P=0.681) were similar between the two groups.

The authors concluded that a treosulfan-based regimen resulted in favorable OS and DFS with acceptable toxicity and low relapse rates compared with busulfan-based conditioning.


Single center study of 56 patients post alloHCT to describe those who had a detectable CMV viral load in their bronchoalveolar lavage fluid.

Thirty-five (62.5%) patients experienced plasma CMV reactivation in the first 100 days. Ten out of 16 BAL samples collected were found to have a detectable CMV viral load.
Six patients were diagnosed with probable CMV pneumonia, all of which had a viral load > 150 copies/mL. Each of the patients had a bronchoalveolar lavage CMV viral load that was higher than that obtained in the plasma, and one patient even had an undetectable plasma level. All were treated initially with ganciclovir or valganciclovir, with 3 requiring addition or change to foscarnet.

Three of the 6 patients showed improvement and an undetectable viral load within 7 days of the start of treatment. The remaining 3 patients died with refractory CMV pneumonia.

Despite the small sample size, the authors concluded that for alloHCT patients, any level of CMV viral load in the BAL could indicate CMV pneumonia, and these patients should receive CMV-directed antiviral therapy.

**Abbreviations**

ALL: acute lymphoid leukemia  
alloHCT: allogeneic hematopoietic cell transplantation  
AML: acute myelogenous leukemia  
ATG: anti-thymocyte globulin  
AUC: area under the curve  
BEAM: carmustine, etoposide, cytarabine, melphalan  
BMFS: bone marrow failure syndrome  
CBT: cord blood transplant  
CLL: chronic lymphocytic leukemia  
CMV: cytomegalovirus; CR, complete remission  
CrCl: creatinine clearance; EFS, event-free survival  
FCR: fludarabine/cyclophosphamide/rituximab  
FDA: Food and Drug Administration  
GVHD: graft versus host disease  
GVL: graft versus leukemia  
HCT: hematopoietic cell transplantation  
IBW: ideal body weight  
MAC: myeloablative conditioning  
MDS: myelodysplastic syndrome  
MMF: mycophenolate mofetil  
MRD: matched related donor  
MUD: matched unrelated donor  
NMA: non-myeloablative  
NRM: non-relapse mortality  
ORR: overall response rate  
OS: overall survival  
PBS: peripheral blood stem cells  
PFS: progression free survival  
SAA: severe aplastic anemia  
TPN: total parenteral nutrition  
TRM: transplant-related mortality

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