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

Allogeneic Transplant

**Allen CE, Marsh R, Dawson P, et al. Reduced-intensity conditioning for hematopoietic cell transplant for HLH and primary immune deficiencies. *Blood*. 2018;132:1438-51.
https://www.ncbi.nlm.nih.gov/pubmed/29997222

- Multicenter, prospective phase 2 trial of reduced-intensity conditioning with melphalan, fludarabine, and intermediate-timing alemtuzumab for patients with HLH or primary immune deficiencies
- Patients aged 4 months through 45 years; 34 patients had diagnosis of HLH and 12 patients carried other primary immune deficiencies
- Median follow-up of 20 months , the 1-year OS was 80.4% (90% CI, 68.6%-88.2%) and 18-month OS of 66.7% (90% CI, 52.9%-77.3%)
- At 1 year, only 39.1% of patients had sustained engraftment without DLI or second HCT; day 100 incidence of grade II-IV acute GVHD was 17.4% and 1-year incidence of chronic GVHD was 26.7%
- Despite showing low early mortality, most surviving patients required DLI or second HCT; future approaches that maintain low early morality are needed

*Yahng Seung-Ah, Park Sung-Soo, Jeon Young-Woo, et al. Successful outcomes of second hematopoietic stem cell transplantation with total nodal irradiation and ATG conditioning for graft failure in adult patients with severe aplastic anemia. *Bone Marrow Transplant.* 2018;53:1270-1277.
https://www.ncbi.nlm.nih.gov/pubmed/?term=29563590

- Retrospective study evaluating the efficacy and safety of a single dose of 750 cGy TNI combined with rabbit ATG 1.25 mg/kg/day for 3 consecutive days after unmanipulated PBSC infusion with a second MSD in 24 adult patients with acquired SAA and graft failure
- Selection criteria for a second transplant for patients experiencing primary or secondary graft failure included an age of <60 years, an ECOG performance status of <2, no major organ failure, donor availability, and the patient preference
- All but 1 patient achieved successful engraftment of neutrophils (median 12 days, range 5-21) and platelets (median 15 days, range 9-316)
- After a median follow-up of 57.4 months (range, 11.2-155.2), the 5-year OS and failure-free survival were 95.7% (95% CI 87.7-100%) and 87.5% (95% CI 75.2-100%), respectively
- This study demonstrated successful outcomes following a second MSD transplant in SAA after graft failure, and the results suggest TNI-750/ATG is a feasible re-conditioning option

Autologous Transplant

*Nguyen VP, Landau H, Quillen K, et al. Modified High-Dose Melphalan and Autologous Stem Cell Transplantation for Immunoglobulin Light Chain Amyloidosis. *Biol Blood Marrow Transplant.* 2018; 24:1823-1827. https://www.ncbi.nlm.nih.gov/pubmed/29933072

- Evaluation of 334 consecutive patients with AL amyloidosis who received modified high-dose melphalan (100-140 mg/m^2) with auto-HCT between 1994-2017
- Seventy percent of patients had involvement in more than 1 organ, 7% were transplant while on dialysis, 32% were older than 65 years, 3% had LVEF <45%, and 87% received melphalan at 140 mg/m^2
- At 1 year, 21% had died, 33% achieved a hematologic CR, 20% VGPR, 25% PR, and 31% had no response
- At 1 year, 38% achieved a cardiac response and 43% achieved a renal response
- Overall median OS was estimated at 6.1 years with EFS of 4.3 years
- Median OS in patients with hematologic CR was 13.4 year, VGPR was 7 years, PR was not reached, and no response was 1.6 years
- Although outcomes seem to be slightly lower than previously reported with full intensity high-dose melphalan, these results are compelling when compared with the transplant ineligible population. These data suggest reduced-dose conditioning remains an effective option for AL amyloidosis patients unable to received full-dose melphalan

*Olivieri J, Mosna F, Pelosini M, et al. A Comparison of the Conditioning Regimens BEAM and FEAM for Autologous Hematopoietic Stem Cell Transplantation in Lymphoma: An Observational Study on 1038 Patients From Fondazione Italiana Linfomi. *Biol Blood Marrow Transplant.* 2018; 24:1814-1822. https://www.ncbi.nlm.nih.gov/pubmed/29857196

- Multicenter, retrospective, cohort study of patient receiving BEAM vs FEAM chemotherapy with autologous transplant between 2008-2015
- The FEAM regimen used the standard BEAM backbone and substituted fotemustine 150 mg/m^2 on days -7 and -6 in place for carmustine
- 1038 patients were included (607 treated with BEAM and 431 with FEAM)
- The most common diagnoses in both groups was aggressive NHL followed by MCL then indolent NHL and the BEAM group had significantly higher HCT-CI driven by rate of pulmonary comorbidities (15.3% vs 10.1%)
- FEAM patients experienced statistically significantly more GI toxicity (mucositis, diarrhea, nausea/vomiting), grade 4 severe infectious events, higher incidence of gram negative and fungal isolates, slightly longer platelet engraftment, and slightly longer hospital stays (21 days with BEAM vs 23 days with FEAM)
- Disease response, OS, PFS, NRM, and relapse were not different between groups.
- FEAM was associated with higher infection related mortality (HR: 1.99; p = 0.04)
- Although response rates were similar between groups, the increase in toxicity limits the usefulness of the FEAM regimen. Authors note that in the circumstance of carmustine shortages, FEAM may be an alternative option.

Cellular Therapy

* Lin JK, Lerman BJ, Barnes JI, et al. Cost Effectiveness of Chimeric Antigen Receptor T-Cell Therapy in Relapsed or Refractory Pediatric B-Cell Acute Lymphoblastic Leukemia . *J Clin Oncol*. 2018 Sep 13. [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/30212291

- Cost effectiveness evaluation of tisagenlecleucel in relapsed or refractory pediatric B-cell ALL from a US health payer perspective over a lifetime horizon. The authors based their assessment and evaluation on three model scenarios: 0%, 20%, 40% 5-year relapse-free survival.
- Markov modeling was informed by recent multicenter, single-arm clinical trials in comparison with blinatumomab, clofarabine combination therapy (clofarabine, etoposide, and cyclophosphamide) and clofarabine monotherapy. Scenario and probabilistic sensitivity analyses were used to explore uncertainty. The main outcomes evaluated were life-years, discounted lifetime costs, QALYs, and incremental cost-effectiveness ratio (3% discount rate).
- Assuming a 40% 5-year RFS rate, tisagenlecleucel increased life expectancies by 12.1 years and cost $61,000/QALY gained.
- Assuming a 20% 5-year RFS rate, tisagenlecleucel increased life expectancies by 3.8 years and cost $151,000/QALY gained.
- Assuming a 0% 5-year RFS rate and use as a bridge to HCT, tisagenlecleucel increased life expectancies by 5.7 years and cost $184,000/QALY gained.
- Reduction of tisagenlecleucel price from $475,000 to $200,000 or $300,000 would allow it to meet a $100,000/QALY or $150,000/QALY willingness-to-pay threshold in all scenarios.
- Based on this study, the long-term effectiveness of tisagenlecleucel is a critical but is an uncertain determinant of its cost effectiveness. At current pricing, tisagenlecleucel represents reasonable value only if it can keep a substantial fraction of patients in remission without HCT; however, if all patients ultimately require HCT to remain in remission, it will not be cost effective at generally accepted thresholds.

*Svoboda J, Rheingold SR, Gill SI, et al. Nonviral RNA chimeric antigen receptor-modified T cells in patients with Hodgkin lymphoma. *Blood*. 2018;132:1022-26.
https://www.ncbi.nlm.nih.gov/pubmed/29925499

- Pilot study of 5 heavily pretreated patients with biopsy-proven relapsed or refractory cHL who failed ≥ 1 salvage therapy and lacked curative options
- Investigational agent was a nonviral RNA CART19 cell expressing an anti-CD19 single-chain variable fragment linked to 4-1BB and CD3-ζ signaling domains
- Patients underwent leukapheresis followed by in vitro T-cell activation and expansion; expanded T-cells were transfected with messenger RNA encoding the anti-CD19 CAR
- Four patients received the protocol-specified cell dose; there were no severe toxicities; responses were seen but were transient
- Manufacturing CART19 by transfecting autologous T-cells with messenger RNA is feasible; targeting CD19+ B cells in cHL using nonviral RNA CART19 was well tolerated

Long-term Complications

*Hefazi M, Langer KJ, Khera N, et al. Extracorporeal Photopheresis Improves Survival in Hematopoietic Cell Transplant Patients with Bronchiolitis Obliterans Syndrome without Significantly Impacting Measured Pulmonary Functions. *Biol Blood Marrow Transplant.* 2018; 24:106-1913.
https://www.ncbi.nlm.nih.gov/pubmed/29679771

- Retrospective, matched cohort study evaluating patients diagnosed with BOS treated with or without ECP
- A total of 1325 patients were initially screened with 88 confirmed diagnoses of BOS per the NIH 2014 criteria; of these 88, 26 were included in each group based on propensity score matching

- BOS was diagnosed at a median of 13-14 months after HCT and ECP was started at a median of 1.5 months after diagnosis
- In the matched ECP group, patient underwent a median of 31 cycles of ECP over a median of 15 months with a pluarality of patients receiving 21-40 cycles
- The rate of corticosteroid and other immunosuppressive therapies at the time of BOS diagnosis were similar between the ECP and non-ECP groups
- At a median follow up of 38 months, the ECP group had significantly longer OS (not reached vs 32 months; p=0.01)
- Fourteen patient (50%) in each group had moderate or severe nonpulmonary cGVHD however the non-ECP population was more likely to remain on >5 mg/day of prednisone at the last outpatient visit (54% vs 23%; p=0.04)
- Multivariate analysis found matched related donors, ECP, and slower rate of FEV decline as independent, favorable prognostic factors for OS
- Rate of PFT decline did not differ between the two groups
- ECP appeared to improve OS in patients with BOS without impacting pulmonary function when compared to propensity matched non-ECP patients. This study was able to provide matched comparative results in a very specific patient population but future clinical trials are needed to further elucidate these results.

Abbreviations

ALL: acute lymphoblastic leukemia
ATG: antithymocyte globulin
auto-HCT: autologous hematopoietic cell transplantation
BEAM: carmustine, etoposide, cytarabine, melphalan
BOS: bronchiolitis obliterans syndrome
CAR: chimeric antigen receptor
cGVHD: chronic graft-versus-host-disease
cHL: classical Hodgkin lymphoma
CR: complete response
DLI: donor lymphocyte infusion
ECP: extracorporeal photopheresis
EFS: even free survival
FEAM: fotemustine, etoposide, cytarabine, melphalan
GI: gastrointestinal
GVHD: graft-versus-host disease
HCT: hematopoietic cell transplant
HCT-CI: hematopoietic cell transplant comorbidity index
HLH: hemophagocytic lymphohistiocytosis
MCL: mantle cell lymphoma
MSD: matched sibling donor
NHL: non-Hodgkin lymphoma
NIH: National Institutes of Health
NRM: non-relapse mortality
OS: overall survival
PBSC : peripheral blood stem cell
PFS: progression-free survival

PFT: pulmonary function tests
PR: partial response
QALYs: discounted quality-adjusted life-years
RFS: relapse-free survival
RNA: ribonucleic acid;
SAA: severe aplastic anemia
TNI: total nodal irradiation
VGPR: very good partial response

ASBMT Pharmacy SIG Communications Working Committee:
Brandi Anders, Tiene Bauters, Eileen Chen, David Eplin, Katie Gatwood, Jason Jared, Kathryn Maples, Shreya Shah, Ryan Shaw