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Stem Cell

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Stem Cell Transplant Research Literatures

Dr. Mark Herbert

World Development Institute
39 Main Street, Flushing, Queens, New York 11354, USA, ma708090@gmail.com

Abstract: Stem cells are derived from embryonic and non-embryonic tissues. Most stem cell studies are for animal stem cells and plants have also stem cell. Stem cells were discovered in 1981 from early mouse embryos. Stem cells have the potential to develop into all different cell types in the living body. Stem cell is a body repair system. When a stem cell divides it can be still a stem cell or become adult cell, such as a brain cell. Stem cells are unspecialized cells and can renew themselves by cell division, and stem cells can also differentiate to adult cells with special functions. Stem cells replace the old cells and repair the damaged tissues. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are thought to be limited to differentiating into different cell types of their tissue of origin. This article introduces recent research reports as references in the related studies.
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Key words: stem cell; transplant; life; research; literature

Introduction

The stem cell is the origin of an organism's life that has the potential to develop into many different types of cells in life bodies. In many tissues stem cells serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a red blood cell or a brain cell. This article introduces recent research reports as references in the related studies.

The following introduces recent reports as references in the related studies.

Aguiar, M., et al. (2021). "Co-production of randomized clinical trials with patients: a case study in autologous hematopoietic stem cell transplant for patients with scleroderma." Trials **22**(1): 611.

BACKGROUND: Increasingly, it is argued that clinical trials struggle to recruit participants because they do not respond to key questions or study treatments that patients will be willing or able to use. This study explores how elicitation of patient-preferences can help designers of randomized controlled trials (RCTs) understand the impact of changing modifiable aspects of treatments or trial design on recruitment. METHODS: Focus groups and a discrete choice experiment (DCE) survey were used to elicit preferences of people with scleroderma for autologous hematopoietic stem cell transplant (AHSCT) treatment interventions. Preferences for seven attributes of treatment (effectiveness, immediate and long-term risk, care team composition and experience, cost, travel distance) were estimated using a mixed-logit model and used to predict participation in RCTs. RESULTS: Two hundred seventy-eight people with scleroderma answered the survey. All AHSCT treatment attributes significantly influenced preferences. Treatment effectiveness and risk of late complications contributed the most to participants' choices, but modifiable factors of distance to treatment center and cost also affected preferences. Predicted recruitment rates calibrated with participation in a recent trial (33%) and suggest offering a treatment closer to home, at lower patient cost, and with holistic, multidisciplinary care could increase participation to 51%. CONCLUSIONS: Through a patient engaged approach to preference elicitation for different features of AHSCT treatment options, we were able to predict what drives the decisions of people with scleroderma to participate in RCTs. Knowledge regarding concerns and the trade-offs people are willing to make can inform clinical study design, improving recruitment rates and potential uptake of the treatment of interest.

Akella, P., et al. (2021). "Toxic 'Toxo' in the heart: Cardiac toxoplasmosis following a hematopoietic stem cell transplant- a case report." IDCases **25**: e01217.

Toxoplasmosis is a rare but potentially severe complication after allogeneic hematopoietic cell transplantation. Toxoplasma gondii-associated cardiac involvement can cause myocarditis, pericarditis, arrhythmias, and congestive heart failure. Most cases

with cardiac toxoplasmosis following BMT have been fatal and diagnosed at autopsy. We present an unfortunate case of sudden onset congestive heart failure symptoms and delayed post-transplant Toxoplasma PCR testing that ultimately led to the diagnosis of cardiac toxoplasmosis on autopsy in our patient.

Alarcon Tomas, A., et al. (2021). "The post-transplant scoring system (PTSS) is associated with outcomes in patients with MDS after CD34+selected allogeneic stem cell transplant." Bone Marrow Transplant.

The post-transplant scoring system (PTSS), developed by the Francophone Society of Bone Marrow Transplantation and Cellular Therapy, is based on three independent post-transplant risk factors: grade of acute graft-versus-host disease, lack of platelet recovery before day 100, and relapse before day 100; discriminating low- (0), intermediate- (1-3), and high-risk (4-8) patients. We investigated the prognostic value of the PTSS in a cohort of patients with MDS who underwent myeloablative CD34-selected TCD transplants. From 2008 to 2018, 109 patients underwent a first TCD-HCT for MDS at our center. We used Cox proportional hazards models and different landmark analyses to evaluate the association of categorized PTSS score risk groups with overall survival (OS). Patients with an intermediate/ high risk PTSS score had decreased OS at day 180 (univariate HR 3.25 [95% CI 1.60, 6.60], $p = 0.001$) and at day 365 (univariate HR 5.42 [95% CI 2.21, 13.3], $p < 0.001$) compared to low risk PTSS scores. This association remained significant after adjusting for HCT-CI. PTSS score calculated at day 100 was not associated with OS, even after adjusting for HCT-CI subgroups. In summary, the PTSS predicted survival at day 180 and day 365 in recipients of T-cell-depleted allografts for myelodysplastic syndrome.

Albanyan, O., et al. (2021). "Impact of pre-transplant induction therapy on outcomes of patients who undergo autologous stem cell transplantation for mantle cell lymphoma in first complete remission." Hematol Oncol Stem Cell Ther.

Mantle cell lymphoma is a rare subtype of non-Hodgkin's lymphoma with poor prognosis and continue to be challenging to treat. The choice of first line induction regimen remains a topic of debate due paucity of clinical trials. We retrospectively evaluated 66 patients diagnosed with mantle cell lymphoma who achieved first complete response after induction chemotherapy followed by autologous stem cell transplant. Treatment groups were divided into low-intensity versus high-intensity regimens. Our data showed the intensity of induction regimen does not impact posttransplant outcomes of mantle cell lymphoma who underwent autologous stem cell transplant in first complete response.

Ali, H. and A. Bacigalupo (2021). "2021 Update on Allogeneic Hematopoietic Stem Cell Transplant for Myelofibrosis: A Review of Current Data and Applications on risk Stratification and Management." Am J Hematol.

Astashchanka, A., et al. (2021). "Pulmonary Complications in Hematopoietic Stem Cell Transplant Recipients-A Clinician Primer." J Clin Med **10**(15).

Hematopoietic stem cell transplants (HSCT) are becoming more widespread as a result of optimization of conditioning regimens and prevention of short-term complications with prophylactic antibiotics and antifungals. However, pulmonary complications post-HSCT remain a leading cause of morbidity and mortality and are a challenge to clinicians in both diagnosis and treatment. This comprehensive review provides a primer for non-pulmonary healthcare providers, synthesizing the current evidence behind common infectious and non-infectious post-transplant pulmonary complications based on time (peri-engraftment, early post-transplantation, and late post-transplantation). Utilizing the combination of timing of presentation, clinical symptoms, histopathology, and radiographic findings should increase rates of early diagnosis, treatment, and prognostication of these severe illness states.

Baertsch, M. A., et al. (2021). "Carfilzomib, Lenalidomide, and Dexamethasone Followed by Salvage Autologous Stem Cell Transplant with or without Maintenance for Relapsed or Refractory Multiple Myeloma." Cancers (Basel) **13**(18).

Salvage high-dose chemotherapy and autologous stem cell transplantation (HDCT/ASCT) is a treatment option for relapsed and/or refractory multiple myeloma (RRMM). No data are available on salvage HDCT/ASCT following re-induction treatment with state-of-the-art triplet regimens. We retrospectively report on 44 patients receiving salvage HDCT/ASCT following re-induction with carfilzomib/lenalidomide/dexamethasone (KRd). All patients received frontline HDCT/ASCT with median time to progression (TTP1) of 2.9 (1.2-13.5) years, enabling paired comparison of frontline and salvage HDCT/ASCT. After re-induction and before salvage transplant, 25/44 patients (57%) attained >/= very good partial response (VGPR), which increased to 34/44 (77%) at best response after salvage HDCT/ASCT. Median progression-free survival (PFS) was 23.3 months from salvage HDCT/ASCT. Patients with >/= VGPR at the time of salvage HDCT/ASCT and those receiving maintenance treatment post salvage HDCT/ASCT had significantly superior PFS (hazard ratio (HR) 0.19, $p = 0.001$ and HR 0.20, $p = 0.009$). In patients achieving at least an equal depth of response before salvage HDCT/ASCT as before frontline HDCT/ASCT, PFS after salvage HDCT/ASCT was

comparable to the frontline situation (p = 0.3). This is the first report of state-of-the-art triplet re-induction and salvage HDCT/ASCT for RRMM after frontline transplantation. Deep remissions achieved with KRd translate into prolonged PFS following salvage HDCT/ASCT and are enhanced by maintenance treatment.

Bangerter, L. R., et al. (2021). "A hybrid method of healthcare delivery research and human-centered design to develop technology-enabled support for caregivers of hematopoietic stem cell transplant recipients." Support Care Cancer.

Health information technology (HIT) is a widely recognized strategy to encourage cancer patients and caregivers to participate in healthcare delivery in a sustainable and cost-effective way. In the context of autologous hematopoietic cell transplant (HSCT), HIT-enabled tools have the potential to effectively engage, educate, support, and optimize outcomes of patients and caregivers in the outpatient setting. This study sought to leverage human-centered design to develop a high-fidelity prototype of a HIT-enabled psychoeducational tool for HSCT caregivers. Phase 1 focuses on breadth and depth of information gathering through a systematic review and semi-structured interviews to determine optimal tool use. Phase 2 engages in human-centered design synthesis and visualization methods to identify key opportunities for the HIT design. Phase 3 employs human-centered design evaluation, engaging caregivers to respond to low-fidelity concepts and scenarios to help co-design an optimal tool for HSCT. This study outlines a hybrid method of healthcare delivery research and human-centered design to develop technology-enabled support for HSCT caregivers. Herein, we present a design methodology for developing a prototype of HIT-enabled psychoeducational tool which can be leveraged to develop future eHealth innovations to optimize HSCT.

Beenet, L. (2021). "Profile of Hepatobiliary Dysfunction in Hematopoietic Stem Cell Transplant Recipients: Autoimmune Diseases Also Contribute." J Clin Exp Hepatol **11**(5): 630-631.

Bewersdorf, J. P., et al. (2021). "Hypomethylating agents and FLT3 inhibitors as maintenance treatment for acute myeloid leukemia and myelodysplastic syndrome following allogeneic hematopoietic stem cell transplant - a systematic review and meta-analysis." Transplant Cell Ther.

BACKGROUND: Disease relapse remains the major cause of death among patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) who receive an allogeneic hematopoietic cell transplant (allo-HCT). Maintenance treatment with FLT3 inhibitors and hypomethylating agents (HMA) has been studied in various clinical trials with mixed results. OBJECTIVE: To synthesize the current evidence on the efficacy and safety of FLT3 inhibitors and HMA for maintenance therapy following allo-HCT in AML and MDS. METHODS: For this systematic review and meta-analysis Cochrane Library, Google Scholar, Ovid Medline, Ovid Embase, PubMed, Scopus, and Web of Science Core Collection were searched from inception to March 2021 for studies on maintenance therapies following allo-HCT in AML and MDS. Studies were excluded if they were reviews, commentaries, case series with <5 patients, or basic research articles, not published in English, not on post-allo-HCT maintenance with FLT3 inhibitors or HMA in AML or MDS, or if they were clinical trials without published results or duplicate publications from the same patient cohort. Studies with insufficient reporting of the primary endpoint (2-year overall survival [OS]) and studies using FLT3 inhibitors or HMA for pre-emptive treatment of imminent relapse based on positive measurable residual disease testing were excluded. Random-effects models were used to pool response rates for the primary outcome of 2-year OS. Hazard ratios (HR) for death and relapse were calculated for studies that included a control group. Rates of relapse-free survival (RFS), non-relapse mortality and acute and chronic graft-versus-host-disease (GVHD) were studied as secondary endpoints. Downs and Black checklist and risk of bias assessments were used to gauge the quality of individual studies. The study protocol has been registered on PROSPERO (CRD42020187298). RESULTS: Our search strategy identified 5559 studies. Twenty-one studies with a total of 809 patients were included in the meta-analysis. 2-year OS rates were 81.7% (95% confidence interval [CI]: 73.8-87.7%) and 65.7% (95% CI: 55.1-74.9%) among patients treated with FLT3 inhibitors and HMA, respectively. In sensitivity analyses restricted to studies that included a control group, maintenance therapy with FLT3 inhibitors (HR for death: 0.41; 95% CI: 0.26-0.62) or HMA (HR: 0.45; 95% CI: 0.31-0.66) appeared superior to no maintenance therapy. 2-year RFS rates were 79.8% (95% CI: 75.0-83.9%) and 62.4% (95% CI: 50.6-72.9%) among patients treated with FLT3 inhibitors and HMA, respectively. Rates of any grade acute and chronic GVHD were 33.1% (95% CI: 25.4-41.8%; grade 3/4: 16.5%) and 42.5% (95% CI: 26.3-60.4%) among FLT3 inhibitor and 42.7% (95% CI: 33.5-52.4%; grade 3/4: 8.1%) and 41.5% (95% CI: 32.0-51.6%) among HMA-treated patients, respectively. CONCLUSION: Maintenance therapy with either FLT3 inhibitors or HMA following allo-HCT, can lead to prolonged and improved OS and RFS with a favorable safety profile. Additional studies are needed to define the optimal duration of treatment, the

role of measurable residual disease status, and transplant characteristics in patient selection.

Bharathi, V., et al. (2020). "Successful Triplet Pregnancy Post-Allogeneic Stem Cell Transplant in a Patient With Doxorubicin-Induced Cardiomyopathy." JACC Case Rep **2**(7): 987-990.

We report the unique case of a patient who recovered cardiac function despite a history of doxorubicin-induced cardiomyopathy, chest radiation therapy, high dose chemotherapy post-allogeneic stem cell transplant, and triplet pregnancy. Data are sparse on doxorubicin-induced cardiomyopathy in pregnant patients, calling for further studies to help formulate management or surveillance recommendations. (Level of Difficulty: Advanced.).

Bryce, A. N., et al. (2021). "Staphylococcus haemolyticus meningitis and bacteremia in an allogenic stem cell transplant patient." IDCases **26**: e01259.

Staphylococcus haemolyticus is a rare cause of bacterial meningitis and most commonly occurs as a nosocomial infection in patients' post-neurosurgery. We report a patient post-allogenic stem cell transplant, with no prior history of neurosurgical procedures, who developed S. haemolyticus meningitis and bacteremia following central catheter-related bloodstream infection. The patient failed therapy with vancomycin and daptomycin but was successfully treated with a prolonged course of linezolid. We review the pharmacological management of coagulase negative Staphylococcus (CoNS) meningitis, with a focus on the pharmacokinetic properties of vancomycin, daptomycin and linezolid within the cerebrospinal fluid (CSF).

Cimpeanu, E., et al. (2021). "Allogeneic hematopoietic stem cell transplant for sickle cell disease: The why, who, and what." Blood Rev: 100868.

Allogeneic hematopoietic stem cell transplants (allo-HSCTs) from matched-related donors (MRDs), mismatched-related donors (MMRDs), and matched-unrelated donors (MUDs) are increasingly being used to treat sickle cell disease (SCD) in both pediatric and adult patients. The overall results have been extremely encouraging, especially if a MRD is available and the transplant being performed before the age of 13. Although there is a general consensus that patients with high-risk SCD, even in adults and irrespective of donor characteristics, should be offered allo-HSCT, the debates on optimal patient selection and timing of transplant have yet to be resolved. Unlike patients with hematologic malignancies, there are also a number of clinical issues that require to be addressed in patients with SCD undergoing allo-HSCT. In this review, we will discuss the reasons allo-HSCT should be offered more widely to patients with SCD, the challenges facing physicians in patient selection and timing of transplant, and the awareness of and solutions to prevent the complications that are unique or more common in SCD undergoing allo-HSCT.

Colton, H., et al. (2021). "Long-term survivors following autologous haematopoietic stem cell transplantation have significant defects in their humoral immunity against vaccine preventable diseases, years on from transplant." Vaccine **39**(34): 4778-4783.

Current international guidelines recommend routinely vaccinating haematopoetic stem cell transplant (HSCT) recipients. Despite significant infection-related mortality following autologous HSCT, routine vaccination programmes (RVP) completion is poor. For recovered HSCT recipients, it is uncertain whether catch-up vaccination remains worthwhile years later. To determine potential susceptibility to vaccine preventable infections, we measured antibody titres in 56 patients, a median of 7years (range 0-29) following autologous HSCT, who had not completed RVP. We found that almost all participants had inadequate titres against diphtheria (98.2%) and pneumococcal infection (100%), and a significant proportion had inadequate titres against measles (34.5%). Of those subsequently vaccinated according to available guidelines, many mounted adequate serological responses. These data suggest a pragmatic catch-up approach for autologous HSCT recipients who have not completed RVP is advisable, with universal vaccination against some pathogens (e.g. Streptococcus pneumoniae and diphtheria) and serologically-guided approaches for others (e.g. measles and varicella zoster virus).

Connelly, J. A. and B. N. Savani (2021). "Finding the best haematopoietic stem cell transplant regimen for GATA2 haploinsufficiency: how close are we?" Br J Haematol.

Davidow, K., et al. (2021). "Pulmonary Outcomes After Autologous Stem Cell Transplant for Hodgkin Lymphoma." J Pediatr Hematol Oncol.

Autologous hematopoietic stem cell transplant (ASCT) may be curative therapy for pediatric patients with relapsed/refractory Hodgkin lymphoma (HL). Therapy for HL may involve pulmonary toxic modalities. Little information exists regarding pulmonary function in these patients post-ASCT. A retrospective chart review was performed for patients undergoing ASCT from February 2012 to December 2019. Lung disease was defined as a z-score </=-1.7 in forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), total lung capacity (TLC), or diffusing capacity of lung for carbon monoxide. Descriptive and limited statistical analyses were performed. Twenty-eight patients were included. Median age at diagnosis was 15 (2 to 19) and was 17 (4 to 21) at ASCT. Twenty-three received radiation before ASCT. Fourteen received brentuximab before, and 9 after, transplant. Nineteen met criteria for lung disease

post-ASCT. Sixteen had lung disease before ASCT. Longitudinal trends for pulmonary function testing parameters did not reach statistical significance, however, FEV1, FVC, and TLC trended towards worsening immediately post-transplant. There was no statistically significant change in FEV1, FVC, or TLC at 2 years as compared with pretransplant data, suggesting no substantial difference from baseline. Diffusing capacity of lung for carbon monoxide showed statistically significant improvement at the 2 year timepoint (P=0.03). This data reinforces the importance of close follow-up for these patients. Large cohort studies are necessary to identify risk factors so that possible mitigative strategies or alternate regimens could be used.

Dulery, R., et al. (2021). "Early Cardiac Toxicity Associated With Post-Transplant Cyclophosphamide in Allogeneic Stem Cell Transplantation." JACC CardioOncol **3**(2): 250-259.

Background: Post-transplant cyclophosphamide (PT-Cy) has become a standard of care in haploidentical hematopoietic stem cell transplantation (HSCT) to reduce the risk of graft-versus-host disease. However, data on cardiac events associated with PT-Cy are scarce. Objectives: This study sought to assess the incidence and clinical features of cardiac events associated with PT-Cy. Methods: The study compared clinical outcomes between patients who received PT-Cy (n = 136) and patients who did not (n = 195), with a focus on early cardiac events (ECE) occurring within the first 100 days after HSCT. All patients had the same systematic cardiac monitoring. Results: The cumulative incidence of ECE was 19% in the PT-Cy group and 6% in the no-PT-Cy group ($p < 0.001$). The main ECE occurring after PT-Cy were left ventricular systolic dysfunction (13%), acute pulmonary edema (7%), pericarditis (4%), arrhythmia (3%), and acute coronary syndrome (2%). Cardiovascular risk factors were not associated with ECE. In multivariable analysis, the use of PT-Cy was associated with ECE (hazard ratio: 2.7; 95% confidence interval: 1.4 to 4.9; $p = 0.002$]. Older age, sequential conditioning regimen, and Cy exposure before HSCT were also associated with a higher incidence of ECE. Finally, a history of cardiac events before HSCT and ECE had a detrimental impact on overall survival. Conclusions: PT-Cy is associated with a higher incidence of ECE occurring within the first 100 days after HSCT. Patients who have a cardiac event after HSCT have lower overall survival. These results may help to improve the selection of patients who are eligible to undergo HSCT with PT-Cy, especially older adult patients and patients with previous exposure to Cy.

Ehlert, K., et al. (2021). "Efficacy of Brincidofovir in Pediatric Stem Cell Transplant Recipients With Adenovirus Infections." J Pediatric Infect Dis Soc.

BACKGROUND: Adenovirus (AdV) infections are of particular concern in pediatric hematopoietic stem cell transplantation (HSCT) recipients as therapeutic options are limited. Brincidofovir (BCV) is the lipid-conjugated pro-drug of cidofovir (CDV) with oral bioavailability and higher intracellular concentrations of the active drug. METHODS: In this retrospective, single-center analysis, we included allogeneic pediatric HSCT recipients with refractory AdV infections because of contraindications or insufficient response to CDV. Common posttransplant viruses were monitored at least weekly by PCR in blood, stool, and urine. RESULTS: Each of the 8 patients received 6 to 12 doses of BCV. BCV treatment was initiated between days +5 and +77. AdV DNAemia and intestinal AdV infection disappeared completely in 6/8 patients. Early AdV DNAemia before day +21 did not result in increased mortality. One patient with a systemic, acyclovir-resistant HSV-1 infection responded rapidly to BCV. Four patients did not survive. AdV infection-related death in 2 patients was accompanied by >1 x 109/mL AdV copy numbers in the blood. Two more patients died of graft-vs-host disease and acute respiratory distress syndrome, respectively, both not related to AdV. CONCLUSIONS: AdV DNAemia and intestinal infection subsided completely in 75% of pediatric HSCT recipients treated with BCV. AdV DNAemia exceeding 1 x 109/mL and a poor lymphocyte recovery of <250/microL were associated with high mortality. Early AdV DNAemia before day +21, however, did not result in a worse outcome. Although access to BCV is currently suspended, further clinical trials are needed to clarify the role of BCV in HSCT recipients with AdV infections and its potential benefit in preventing AdV DNAemia in immunocompromised patients.

Fernandez-Caballero, M., et al. (2021). "Impact of risk scores in outcome of patients with myeloid neoplasms after allogeneic stem cell transplant." Med Clin (Barc).

BACKGROUND: The main causes of failure of allogeneic hematopoietic stem cell transplantation (allo-transplant) in patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are relapse and transplant-related mortality. Different scores have been designed to predict the prognosis of these patients. The objective of this study was to assess which score or combination has better outcome predictive capacity. METHODS: Retrospective analysis of patients with AML and MDS who received a first peripheral blood allo-transplant in a single center, between December 2001 and October 2019. Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), European Group for Blood and

Marrow Transplantation (EBMT) and Disease Risk Index (DRI) scores were calculated. For each score and for the HCT-CI/DRI and HCT-CI/EBMT combinations, overall survival (OS), cumulative incidence of relapse (CIR), non-relapse-related mortality (NRM), and graft versus host disease-free relapse-free survival (GRFS) were analyzed. RESULTS: 175 patients were evaluated. With a median (range) follow-up of 3.96 (0.32-17.22) years, the 5-year probabilities (95% CI) of OS, CIR, NRM, and GRFS were 36% (28%-44%), 28% (21%-35%), 38% (30%-46%) and 24% (17%-31%), respectively. For OS, only the DRI score selected two groups with statistically significant differences (DRI 0-1: 41% vs. DRI >/=2: 24%; p=0.011). The combination of DRI 0-1 and HCT-CI 0-2 showed OS probabilities of 45% vs. 26% for those with DRI 0-1 and HCT-CI >/=3; p=0.041. CONCLUSIONS: In patients with AML and MDS submitted to allo-transplant, the combination of HCT-CI and DRI scores provided the best stratification for OS.

Gassas, R. S., et al. (2021). "Early infection in post-autologous hematopoietic stem cell transplant patients: Princess Noorah Oncology Center experience." Saudi Med J **42**(8): 847-852.

OBJECTIVES: To assess local epidemiology and risk factors for bacterial, fungal, and viral infections among the autologous bone marrow transplant population. METHODS: This study is a retrospective correlational cohort design comprising 150 adult patients who underwent autologous transplants at Princess Noorah Oncology Center, Jeddah, Saudi Arabia between 2014 and 2020. RESULTS: The study findings indicate that bacterial infection prevalence differed significantly across the different disease status pre-salvage as patients with the relapsed disease were more likely to have bacterial infections. The median of engraftment days differed significantly between those who had a bacterial infection and those who did not. Interestingly, previous pneumonia infection had a positive relationship with the number of hospital stays. CONCLUSIONS: Bacterial infections are the dominant type of infection among the autologous patient population. The research reflects authentic practice and reports unique characteristics of autologous transplant patients in terms of the prevalence and types of infection these patients experience.

George, E. and M. Manrai (2021). "Response to 'Profile of Hepatobiliary Dysfunction in Hematopoietic Stem Cell Transplant Recipients: Autoimmune Diseases Also Contribute'." J Clin Exp Hepatol **11**(5): 632.

Gonzalez-Villarreal, G., et al. (2021). "First-line haploidentical stem cell transplantation in children and adolescents with severe aplastic anemia using mobilized peripheral blood as source of CD34+: Single-institutional experience in a transplant center from northeast Mexico." Pediatr Transplant: e14082.

INTRODUCTION: The only curative treatment for severe aplastic anemia in children is an allogeneic stem cell transplant; however, few patients have a matched related or unrelated donor. Haploidentical stem cell transplantation (haplo-SCT) using bone marrow (BM) and peripheral blood stem cells (PBSC) has been recently described as effective and safe. In this study, we retrospectively report the outcome of twelve pediatric patients who underwent haplo-SCT using only PBSC. METHODS: The conditioning regimen consisted on rabbit anti-thymocyte globulin (r-ATG) 2.5 mg/kg/d on days -7, -6,-5, and -4, and cyclophosphamide (Cy) 50 mg/kg/d on days -3 and -2. We used Cy 50 mg/kg/d on days +3 and +4, tacrolimus and mycophenolic acid as graft versus host disease (GVHD) prophylaxis. RESULTS: The median follow-up was 1,099 days (45-1258 days). The overall survival rate up-to-date is 83.3%. In 10 of the 12 patients, a sustained graft was achieved. None of the patients had acute or chronic GVHD. CONCLUSIONS: Haplo-SCT could be established as a first-line treatment when there is no matched related or unrelated donor. According to this short sample and previous reports, PBSC are a feasible option effectively used as the sole source of stem cells. Additionally, post-transplant cyclophosphamide remains a good strategy for GVHD prevention.

Gournay, V., et al. (2021). "Outcome of allogeneic hematopoietic stem cell transplant recipients admitted to the intensive care unit with a focus on haploidentical graft and sequential conditioning regimen: results of a retrospective study." Ann Hematol.

Haploidentical transplantation has extended the availability of allogeneic hematopoietic stem cell transplant (alloHCT) to almost all patients. Sequential conditioning regimens have been proposed for the treatment of hematological active disease. Whether these new transplantation procedures affect the prognosis of critically ill alloHCT recipients remains unknown. We evaluated this question in a retrospective study including consecutive alloHCT patients admitted to the intensive care unit of a tertiary academic center from 2010 to 2017. During the study period, 412 alloHCTs were performed and 110 (27%) patients-median age 55 (36-64) years-were admitted to ICU in a median time of 58.5 (14-245) days after alloHCT. Twenty-nine (26%) patients had received a haploidentical graft and 34 (31%) a sequential conditioning. Median SOFA score was 9 (6-11). Invasive mechanical ventilation (MV) was required in 61 (55%) patients. Fifty-six (51%) patients died in the hospital. Independent factors associated with in-hospital mortality were as follows: MV (OR=8.44

[95% CI 3.30-23.19], p<0.001), delta SOFA between day 3 and day 1 (OR=1.60 [95% CI 1.31-2.05], p<0.0001), and sequential conditioning (OR=3.7 [95% CI 1.14-12.92], p=0.033). Sequential conditioning was also independently associated with decreased overall survival (HR=1.86 [95% CI 1.05-3.31], p=0.03). Other independent factors associated with reduced overall survival were HCT-specific comorbidity index >/=2 (HR=1.76 [95% CI 1.10-2.84], p=0.02), acute GVHD grade >/=2 (HR=1.88 [95% CI 1.14-3.10], p=0.01), MV (HR=2.37 [95% CI 1.38-4.07, p=0.002), and vasopressors (HR=2.21 [95% CI 1.38-3.54], p=0.001). Haploidentical transplantation did not affect outcome. Larger multicenter studies are warranted to confirm these results.

Gowda, L. and S. Seropian (2021). "Life Expectancy After Allogeneic Stem Cell Transplant-In It for the Long Haul?" JAMA Oncol.

Guolo, F., et al. (2021). "Pre-transplant minimal residual disease assessment and transplant-related factors predict the outcome of acute myeloid leukemia patients undergoing allogeneic stem cell transplantation." Eur J Haematol.

We studied pretransplant minimal residual disease (MRD) in 224 patients (median age 44 years; range 17-65) with acute myeloid leukemia (AML) undergoing allogeneic stem cell transplant (HSCT) in complete remission. MRD was evaluated on marrow samples using multicolor flow cytometry and assessment of WT1 gene expression. Both methods showed a strong prognostic value and their combination allowed the identification of three groups of patients with different risk of relapse. In multivariate analysis, combined MRD was the only predictor of cumulative incidence of relapse, regardless of donor type, conditioning regimen, first or second CR at HSCT, HSCT year, and ELN risk group. Multivariate regression model showed that only negative combined MRD status (P < .001) and myeloablative conditioning (P = .004) were independently associated with better OS. Among MRD-positive patients, a reduced incidence of relapse was observed in patients receiving haplo transplant (P < .05) and in patients who showed grade II-IV aGVHD (P < .03). In patients with negative combined MRD, the intensity of conditioning regimen did not affect the overall favorable outcome. We suggest that pretransplant MRD evaluation combined with transplant-related factors can identify AML patients at higher risk for relapse and might help in defining the overall transplant strategy.

Halahleh, K., et al. (2021). "The impact of post-hematopoietic stem cell transplant tyrosine kinase inhibitors in Philadelphia-positive acute lymphoblastic leukemia." Hematol Oncol Stem Cell Ther.

Haldorai, M., et al. (2021). "Tumefactive demyelination in pediatrics: An unusual late neurological complication of hematopoietic stem cell transplant." Pediatr Blood Cancer **68**(11): e29318.

Immune-mediated demyelination is a rare posttransplant complication. Here, we report an 8.5-year-old boy who developed left hemiparesis, 18 months post matched sibling donor hematopoietic stem cell transplant (HSCT) for relapsed acute myeloid leukemia and was diagnosed to have tumefactive demyelination. The diagnosis was established based on clinical and radiological features. The complete resolution of the lesions with steroids further established the immune-mediated pathophysiology.

Horowitz, J. G., et al. (2021). "Early antimicrobial prophylaxis in autologous stem cell transplant recipients: Conventional versus an absolute neutrophil count-driven approach." Transpl Infect Dis **23**(4): e13689.

BACKGROUND: Autologous hematopoietic stem cell transplantation (HSCT) recipients are at increased risk of developing life-threatening infections. There is discordance in published recommendations for timing of pre- and post-transplant antimicrobial prophylaxis in this patient population, and these recommendations are unsubstantiated by any published comparative analyses. METHODS: An observational, pre- and post-intervention study of consecutive autologous HSCT recipients was conducted over a 2-year period. In the pre-intervention cohort, antimicrobial prophylaxis was initiated on the day prior to transplant. In the post-intervention cohort, antimicrobials were initiated once absolute neutrophil count (ANC) reached </=500 cells/mm(3) . The primary outcome assessed was frequency of febrile occurrences. Secondary outcomes included total days of prophylaxis, positive blood cultures, all-cause mortality, Clostridioides difficile infection rates, and length of stay. RESULTS: A total of 208 patients were included in the final analysis, with 105 and 103 patients in the pre- and post-intervention cohorts, respectively. The majority of patients included were male. Lower rates of fever occurrences were observed in the post-intervention cohort (83% pre- vs. 69% post-intervention; p = 0.019). A significant reduction in the mean antibacterial days per patient was identified (9.7 vs. 4.6 days; p < 0.001). Other than lower rates of febrile neutropenia in the post-intervention cohort, no differences were identified in secondary outcomes. In multivariable analyses, ANC-driven prophylaxis was independently associated with decreased febrile events. CONCLUSIONS: Delaying prophylaxis until severe neutropenia was not associated with increased febrile events or other secondary clinical outcomes evaluated. This approach is associated with a significant reduction in antimicrobial exposure.

Iwamuro, M., et al. (2021). "Desquamative esophagitis followed by esophageal cancer in a stem cell transplant recipient." Gastrointest Endosc.

Jain, A., et al. (2021). "Does Mesenchymal Stromal Cell Count in Pre-autologous Hematopoietic Stem Cell Transplant Peripheral Blood and Apheresis Product Predict for Infectious Complications in the Post-transplant Period?" Indian J Hematol Blood Transfus **37**(3): 484-488.

Mesenchymal stromal cells (MSC) have gained attention in the recent past considering their multipotentiality and organ-healing properties. Exogenous administration of MSC in the pre-hematopoietic stem cell transplant (HSCT) setting has been reported to enhance engraftment, heal graft-vs-host disease and increase infections in the post-HSCT period. In this study, we aimed to determine the effect of endogenous pre-HSCT MSC on the post-HSCT infectious complications in patients undergoing autologous-HSCT. The study included patients undergoing autologous-HSCT (n = 25; multiple myeloma-20, lymphoma-5). MSC were analyzed and quantified by flow cytometry in the peripheral blood (PB) at baseline, and in both PB and apheresis product (AP) following mobilization with growth factors. Pre-HSCT MSC (PB/AP) were correlated with the post-HSCT duration of febrile neutropenia and duration of antimicrobial drugs using Pearson's correlation co-efficient, and with the mucositis grade using Spearman's rank correlation. Pre-HSCT MSC (baseline and post-mobilization) correlated positively with the longer duration of febrile neutropenia and duration of antimicrobials used in the post-HSCT period ($p < 0.05$). Pre-HSCT MSC failed to correlate with post-HSCT engraftment and onset/severity/duration of oral and gastrointestinal mucositis. Endogenous pre-HSCT MSC counts might predict for increased infectious complications in the post autologous-HSCT setting.

Jamy, O., et al. (2021). "Phase II clinical trial of one dose of post-transplant cyclophosphamide for graft versus host disease prevention following myeloablative, peripheral blood stem cell, matched-unrelated donor transplantation." Am J Hematol **96**(10): E396-E398.

Janssen, M. J. M., et al. (2021). "Predictive factors for vaccine failure to guide vaccination in allogeneic hematopoietic stem cell transplant recipients." Bone Marrow Transplant.

Vaccination after hematopoietic stem cell transplantation (HSCT) is essential to protect high-risk patients against potentially lethal infections. Though multiple studies have evaluated vaccine specific responses, no comprehensive analysis of a complete vaccination schedule post-HSCT has been performed and little is known about predictors for vaccine failure. In this context, allogeneic HSCT (alloHSCT) patients were included and vaccinated starting one year post-transplantation. Antibody responses were measured by Multiplex Immuno Assay for pneumococcal (PCV13), meningococcal C, diphtheria, pertussis, tetanus and Haemophilus influenza type b one month after the last vaccination and correlated to clinical and immunological parameters. Vaccine failure was defined as antibody response above vaccine-specific cut-off values for less than four out of six vaccines. Ninety-six patients were included of which 27.1% was found to have vaccine failure. Only 40.6% of all patients responded adequately to all six vaccines. In multivariate analysis, viral reactivation post-HSCT (OR 6.53; P = 0.03), B-cells <135 per mm(3) (OR 7.24; P = 0.00) and NK-cells <170 per mm(3) (OR 11.06; P = 0.00) were identified as predictors for vaccine failure for vaccination at one year post-alloHSCT. Measurement of antibody responses and an individualized approach for revaccination guided by clinical status and immune reconstitution of B-cells and NK-cells may improve vaccine responses.

Jayani, R. V. and R. L. Olin (2021). "Physically "fit" for allogeneic stem cell transplant?" Bone Marrow Transplant.

Jullien, M., et al. (2021). "Impact of allogeneic stem cell transplantation comorbidity indexes after haplotransplant using post-transplant cyclophosphamide." Cancer Med.

BACKGROUND: Three different scoring systems have been developed to assess pre-transplant comorbidity in allogeneic hematopoietic stem cell transplantation (Allo-HSCT): the Hematopoietic Cell Transplantation-Specific Comorbidity Index, the Comorbidity/Age index, and the Augmented Comorbidity/Age index. All were devised to predict overall survival (OS) and disease-free survival (DFS) survivals and non-relapse mortality (NRM) in patients receiving HLA-matched Allo-HSCT, but their performance has scarcely been studied in the haploidentical Allo-HSCT setting with post-transplant cyclophosphamide, a procedure in constant expansion worldwide. METHODS: To address this issue, their impact on survivals and NRM was examined in a cohort of 223 patients treated with haploidentical Allo-HSCT in four different centers. RESULTS: With a median follow-up of 35.6 months, 3-year OS, DFS, and NRM were 48.1% +/- 4%, 46.3% +/- 4%, and 30.0% +/- 3%, respectively. No impact was found for any of the three comorbidity scores in univariate analysis. In multivariate analyses, the only three factors associated with lower OS were DRI ($p < 0.001$), an older age of recipients (>/=55 years old, $p = 0.02$) and of donors (>/=40 years old, $p = 0.005$). Older donor age was also associated with lower DFS and higher NRM. CONCLUSION: The comorbidity scores do not predict survivals nor NRM in haploidentical Allo-HSCT with

PTCY, suggesting that pre-transplant comorbidities should not be a contra-indication to this procedure.

Kacar, M., et al. (2021). "Frosted Branch Angiitis Associated With Cytomegalovirus in a Pediatric Autologous Stem Cell Transplant Patient: Case Report and Review of the Literature." J Pediatr Hematol Oncol.

BACKGROUND: Frosted branch angiitis (FBA) is a rare phenomenon of panuveitis which may occur secondary to cytomegalovirus (CMV) causing acute visual disturbances. CMV infection is a known complication in allogenic stem cell transplant (SCT) patients but is uncommon following autologous SCT. OBSERVATION: We describe a 17-month-old medulloblastoma patient with sudden onset visual impairment following second autologous SCT. The patient was CMV seropositive, polymerase chain reaction negative before second SCT. At the time of presentation with visual complaints, the patient was diagnosed with FBA associated with CMV reactivation. Treatment included antivirals and immunosuppressive medication with visual recovery. CONCLUSION: FBA induced by CMV should be considered as a differential diagnosis in pediatric patients undergoing autologous bone marrow transplant with rapidly progressive visual impairment.

Karri, P. V., et al. (2021). "Disseminated atypical mycobacterial infection in an allogeneic stem cell transplant recipient." Dermatol Online J **27**(6).

Nontuberculous mycobacteria are pathogens with diverse manifestations in immunocompromised hosts. The lesser-known Mycobacterium haemophilum usually causes cutaneous infection. Diagnosis is challenging but is aided by molecular testing and multidisciplinary communication. We present an immunocompromised patient with disseminated cutaneous mycobacterial infection with digital tenosynovitis.

Khan, S., et al. (2021). "Pediatric high risk neuroblastoma with autologous stem cell transplant - 20 years of experience." Int J Pediatr Adolesc Med **8**(4): 253-257.

Background and Objective: Neuroblastoma is the most common extracranial solid tumor found in pediatric patients. High-risk neuroblastoma (HR-NBL) can be characterized by metastasis, age, and other tumor characteristics that result in an adverse outlook for this patient cohort. The standard of care includes induction chemotherapy, surgery, followed by stem cell autologous transplant (ASCT), and later, antidisialoganglioside (anti-GD2) antibodies. In this study, we provide the survival and toxicity data of our HR-NBL patients treated with a single ASCT. Methods: We retrospectively analyzed pediatric HR-NBL patients treated with single ASCT after a carboplatin, etoposide, and melphalan (CEM) regimen in our institution between January 1993 and December 2014. Results: There were 99 evaluable patients with male predominance. The median age at diagnosis was 3 years. Most of our HR-NBL patients were stage 4 (88%). All patients received ASCT. Peripheral blood was the graft source in 58% of the patients. Time for hematological count recovery with bone marrow as a graft source was prolonged but not statistically significant when compared with PBSCs. Of all the patients, 58% received radiation therapy to residual disease. Overt secondary leukemia was not seen in any of these patients. Three-year overall survival (OS) was 68.5% +/- 5.2% and the 3-year event-free survival (EFS) was (48.3% +/- 5.2%). Conclusion: Our HR-NBL patients tolerated high-dose chemotherapy well followed by single autologous stem cell transplant. Tandem transplant is a feasible option in our patient cohort. Apart from secondary solid tumors, there were no long-term complications seen.

Khouri, I. F., et al. (2021). "Nine-Year Follow-up of Patients with Relapsed Follicular Lymphoma after Nonmyeloablative Allogeneic Stem Cell Transplant and Autologous Transplant." Clin Cancer Res.

PURPOSE: To compare outcomes between patients with relapsed follicular lymphoma who received a nonmyeloablative allogeneic stem cell transplant (alloSCT) and those who received an autologous transplant (autoSCT). PATIENTS AND METHODS: We evaluated 194 patients with follicular lymphoma who received an alloSCT (n = 98) or autoSCT (n = 96) at MD Anderson Cancer Center (Houston, TX). The transplant type used was based on donor availability and by Medicare reimbursement guidelines. Patients who received an alloSCT were enrolled in four consecutive trials in which they received fludarabine, cyclophosphamide (or bendamustine), and rituximab conditioning. autoSCT patients received R-BEAM (rituximab, carmustine, etoposide, cytarabine, and melphalan). RESULTS: The median follow-up of survivors was 108 months for the alloSCT group and 102 months for the autoSCT group. Overall survival was significantly better for patients who received an alloSCT compared with those who received an autoSCT (62% vs. 46%; P = 0.048). Similarly, progression-free survival rates were 52% in patients who received an alloSCT and 31% in those who received an autoSCT (P < 0.001), and the 8-year relapse rates were 11% and 43%, respectively (P < 0.0001). Only three patients in the alloSCT group relapsed beyond 3.5 years. In the alloSCT group, the rates for grade 2 to 4 acute graft-versus-host disease (GVHD), grade 3 to 4 acute GVHD, and extensive chronic GVHD were 22%, 9%, and 38%, respectively. In the autoSCT group, the 8-year incidence of secondary myelodysplasia was 11%. Nonrelapse mortality was similar between the two groups (15% vs.

11% at 8 years; P = 0.27). CONCLUSIONS: This study shows that alloSCT is curative and confers superior survival compared with autoSCT in patients with follicular lymphoma.

Khurana, A., et al. (2021). "Lines of therapy before autologous stem cell transplant and CAR-T affect outcomes in aggressive Non-Hodgkin's lymphoma." Am J Hematol **96**(10): E386-E389.

Kimura, S. I., et al. (2021). "Cytomegalovirus reactivation is associated with an increased risk of late-onset invasive aspergillosis independently of grade II-IV acute graft-versus-host disease in allogeneic hematopoietic stem cell transplantation: JSTCT Transplant Complications Working Group." Ann Hematol.

There is a matter of debate about the clinical impact of cytomegalovirus (CMV) reactivation on the development of late-onset invasive aspergillosis (IA), which occurs 40 days or later after allogeneic hematopoietic stem cell transplantation (HSCT). Using a Japanese transplant registry database, we analyzed the risk factors for the development of late-onset IA in 21,015 patients who underwent their first allogeneic HSCT between 2006 and 2017. CMV reactivation was defined as the initiation of preemptive anti-CMV antiviral therapy. Overall, there were 582 cases of late-onset IA, which occurred at a median of 95 days after HSCT. The 2-year cumulative incidence was 3.4% (95% confidence interval (CI), 3.0-3.9) in patients with CMV reactivation within 40 days after HSCT and 2.5% (95% CI, 2.3-2.8) in those without it (P < 0.001). In a multivariate analysis, CMV reactivation as a time-dependent covariate was significantly associated with the development of late-onset IA (hazard ratio (HR) 1.40, P < 0.001), as well as grade II-IV acute GVHD, age > 50 and HCT-CI >/= 3 in the entire cohort. If we focus on the subgroup without grade II-IV acute GVHD, which is generally an indication for systemic corticosteroid therapy (n = 12,622), CMV reactivation was still a significant factor for the development of late-onset IA (HR 1.37, P = 0.045) as well as age > 50 years, HCT-CI >/= 3, and cord blood transplantation. In conclusion, CMV reactivation was associated with an increased risk of late-onset IA after allogeneic HSCT independently of acute GVHD. Close monitoring for late-onset IA is necessary for patients who develop CMV reactivation even without grade II-IV acute GVHD.

Klippenstein, A. D. W., et al. (2021). "Growth in the face of overwhelming pressure: A narrative review of sibling donor experiences in pediatric hematopoietic stem cell transplant." J Child Health Care: 13674935211043680.

Sibling donation in pediatric hematopoietic stem cell transplant (HSCT) can be emotionally distressing for children, but may simultaneously evoke positive emotions, and has the potential to facilitate personal growth. We conducted a narrative review of sibling donor experiences, which included an analysis of psychosocial distress and post-traumatic growth (PTG). We searched the following databases: MEDLINE, CINAHL, PsycInfo, and SCOPUS. Search concepts used to develop key terms included HSCT, siblings, children, and psychosocial outcomes. Specific inclusion criteria included a) research articles published in English in peer-reviewed journals until September 2020, and b) reported trauma symptoms and PTG characteristics of sibling donation experiences. Four themes were identified: fear and anxiety related to HLA testing, overwhelming pressure to donate, guilt and blame when the ill child died, as well as emotional and physical isolation following donation. Sibling responses also included evidence of PTG, articulated as a deepened appreciation for life, closer relationships with the ill child and other family members, increased personal strength, and spiritual growth. These results highlight a critical need for future research approaches that further empower sibling donor voices, such as those found in participatory, arts-based methodologies.

Kouidhi, S., et al. (2021). "High Throughput Analysis Reveals Changes in Gut Microbiota and Specific Fecal Metabolomic Signature in Hematopoietic Stem Cell Transplant Patients." Microorganisms **9**(9).

There is mounting evidence for the emerging role of gut microbiota (GM) and its metabolites in profoundly impacting allogenic hematopoietic stem cell transplantation (allo-HSCT) and its subsequent complications, mainly infections and graft versus host-disease (GvHD). The present study was performed in order to investigate changes in GM composition and fecal metabolic signature between transplant patients (n = 15) and healthy controls (n = 18). The intestinal microbiota was characterized by NGS and gas chromatography-mass spectrometry was employed to perform untargeted analysis of fecal metabolites. We found lower relative abundances of Actinobacteria, Firmicutes, and Bacteroidetes and a higher abundance of Proteobacteria phylum after allo-HSCT. Particularly, the GvHD microbiota was characterized by a lower relative abundance of the short-chain fatty acid-producing bacteria, namely, the Feacalibacterium, Akkermansia, and Veillonella genera and the Lachnospiraceae family, and an enrichment in multidrug-resistant bacteria belonging to Escherichia, Shigella, and Bacteroides. Moreover, network analysis showed that GvHD was linked to a higher number of positive interactions of Blautia and a significant mutual-exclusion rate of Citrobacter. The fecal metabolome was dominated by lipids in the transplant group when compared with the healthy individuals (p < 0.05). Overall, 76 metabolites were significantly altered within transplant recipients, of which 24 were

selected as potential biomarkers. Furthermore, the most notable altered metabolic pathways included the TCA cycle; butanoate, propanoate, and pyruvate metabolisms; steroid biosynthesis; and glycolysis/gluconeogenesis. Specific biomarkers and altered metabolic pathways were correlated to GvHD onset. Our results showed significant shifts in gut microbiota structure and fecal metabolites characterizing allo-HSCT.

Lazaryan, A., et al. (2021). "Impact of cytogenetic abnormalities on outcomes of adult Philadelphia-negative acute lymphoblastic leukemia after allogeneic hematopoietic stem cell transplantation: a study by the Acute Leukemia Working Committee of the Center for International Blood and Marrow Transplant Research." Haematologica **106**(8): 2295-2296.

Le Bourgeois, A., et al. (2021). "Safety and Antibody Response After 1 and 2 Doses of BNT162b2 mRNA Vaccine in Recipients of Allogeneic Hematopoietic Stem Cell Transplant." JAMA Netw Open **4**(9): e2126344.

Lew, T. E., et al. (2021). "T-cell replete allogeneic stem cell transplant for mantle cell lymphoma achieves durable disease control, including against TP53-mutated disease." Bone Marrow Transplant.

Linnik, J., et al. (2021). "Association of host factors with antibody response to seasonal influenza vaccination in allogeneic hematopoietic stem cell transplant (HSCT) patients." J Infect Dis.

BACKGROUND: Influenza vaccination efficacy is reduced after hematopoietic stem cell transplantation (HSCT) and patient factors determining vaccination outcomes are still poorly understood. METHODS: We investigated the antibody response to seasonal influenza vaccination in 135 HSCT patients and 69 healthy volunteers (HVs) in a prospective observational multicenter cohort study. We identified patient factors associated with hemagglutination inhibition titers against A/California/2009/H1N1, A/Texas/2012/H3N2, and B/Massachusetts/2012 by multivariable regression on the observed titer levels and on seroconversion/seroprotection categories for comparison. RESULTS: Both regression approaches yield consistent results but regression on titers estimated associations with higher precision. HSCT patients required two vaccine doses to achieve average responses comparable to a single dose in HVs. Pre-vaccination titers were positively associated with time after transplantation, confirming that HSCT patients can elicit potent antibody responses. However, an unrelated donor, absolute lymphocyte counts below the normal range and treatment with calcineurin inhibitors lower the odds of responding. CONCLUSIONS: HSCT patients show a highly heterogeneous vaccine response, but overall, patients benefited from the booster shot and can acquire seroprotective antibodies over the years after transplantation. Several common patient factors lower the odds of responding, urging to identify additional preventive strategies in the poorly responding groups.

Marques, A., et al. (2021). "Assessment of quality of life three years from hematopoietic stem cell transplant." Rev Esc Enferm USP **55**: e20200270.

OBJECTIVE: To assess the domains of quality of life related to hematologic cancer patient health in the first three years from autologous and allogeneic hematopoietic stem cell transplantation. METHOD: A prospective cohort from September 2013 to February 2019 at a reference service in Latin America with 55 patients. The instruments Quality of Life Questionnaire Core C30 and Functional Assessment Cancer Therapy - Bone Marrow Transplantation were used. For data analysis, Generalized Linear Mixed Model was used. RESULTS: The domains global and overall quality of life presented the lowest scores in the pancytopenia phase: 59.3 and 91.4 in autologous, 55.3 and 90.3 in allogeneic. The mixed method analysis has shown that there was a significant change in scores between the phases throughout the treatment ($p< 0.05$). CONCLUSION: Health-related quality of life presented significant changes in the domains between the phases throughout time. Understanding these results enables nursing interventions directed at the domains which were damaged during treatment.

Mekelenkamp, H., et al. (2021). "Specialized Pediatric Palliative Care Services in Pediatric Hematopoietic Stem Cell Transplant Centers." Children (Basel) **8**(8).

Hematopoietic stem cell transplantation (HSCT) is widely used in pediatric patients as a successful curative therapy for life-threatening conditions. The treatment is intensive, with risks of serious complications and lethal outcomes. This study aimed to provide insight into current data on the place and cause of death of transplanted children, the available specialized pediatric palliative care services (SPPCS), and what services HSCT professionals feel the SPPCS team should provide. First, a retrospective database analysis on the place and cause of death of transplanted pediatric HSCT patients was performed. Second, a survey was performed addressing the availability of and views on SPPCS among HSCT professionals. Database analysis included 233 patients of whom the majority died in-hospital: 38% in the pediatric intensive care unit, 20% in HSCT units, 17% in other hospitals, and 14% at home or in a hospice (11% unknown). For the survey, 98 HSCT professionals from 54 centers participated. Nearly all professionals indicated that HSCT patients should have access to SPPCS, especially for pain management, but less than half routinely referred to this service at an early stage. We, therefore, advise HSCT teams to

integrate advance care planning for pediatric HSCT patients actively, ideally from diagnosis, to ensure timely SPPCS involvement and maximize end-of-life preparation.

Miles, B. and J. D. Mackey (2021). "Increased Risk of Second Primary Malignancy and Mortality at ten Years After Stem Cell Transplant for Multiple Myeloma: An Analysis of 14,532 Patients." Cureus **13**(7): e16372.

Background The landscape for patients with multiple myeloma has improved dramatically over the last 15 years. Immunomodulatory imide drugs (IMiDs) have shown great efficacy in both the setting of initial therapy and as maintenance after autologous stem cell transplant (ASCT). Concern has arisen, however, regarding the risk of second primary malignancies (SPMs) that appear to be associated with the use of IMiD agents. SPMs are a known sequela of multiple myeloma treatment, particularly as a consequence of maintenance lenalidomide status-post stem cell transplant (SCT). The benefit of SCT has become less clear with the utilization of newer, more effective initial therapies. Objectives To determine the effect of SCT on SPM risk and overall survival in multiple myeloma patients at 5 and 10 years after treatment initiation. Methods We used TriNetX, a global federated health research network providing access to electronic medical records (diagnoses, procedures, medications, laboratory values, genomic information) from approximately 58 million patients in 49 large healthcare organizations. We created two patient cohorts who had all received treatment with thalidomide, lenalidomide, or pomalidomide. One cohort had received SCT while the other had not. Both cohorts were then analyzed for the development of all non-myeloma malignancies which occurred at least one year after initiation of treatment. Results At 5 years, SPMs were 5.8% more likely in patients who received stem cell transplant (22.4% vs 16.6%, RR 0.741, p value <0.0001) but 5-year survival favored transplanted patients by 2.38% (64.85% vs 62.474%, p value 0.0044). 10-year survival favored patients who did not receive transplant by 1.44% (42.279% vs 40.838%, p value 0.0279). The Kaplan-Meier curves cross at year 6. Conclusions It has previously been shown that the use of alkylating agents in myeloma patients significantly increases the risk of SPM, but that difference had curiously not been shown to have a negative impact on survival. Our analysis shows that this negative survival impact does exist but requires six or more years of follow up to become evident. Recent analyses from studies using older regimens show no overall survival benefit from the use of stem cell transplant. As non-transplant regimens become more effective at producing minimal residual disease (MRD) negativity, it seems that transplantation for myeloma patients will soon be regarded as unnecessary or even detrimental.

Miranda-Silva, W., et al. (2021). "Oral shedding of herpesviruses and clinical outcomes in hematopoietic stem cell transplant patients." Oral Dis.

OBJECTIVES: To characterize the oral shedding of herpes viruses in patients who underwent allogeneic hematopoietic stem cell transplantation (alloHSCT) and investigate its relationship with clinical outcomes. MATERIALS AND METHODS: Polymerase chain reaction and enzymatic digestion were performed to identify the oral shedding of the members of the Herpesviridae family in 31 patients. The samples were collected from the oral cavity at five timestamps. RESULTS: The presence of each herpesvirus in the oral cavity was observed in 3.2%, 12.9%, 19.3%, 32.2%, 54.8% and 93.5% patients for human herpesvirus (HHV)-6A, herpes simplex virus-1, HHV-6B, cytomegalovirus (CMV), Epstein-Barr virus (EBV) and HHV-7, respectively. Oral shedding of herpes virus was not uncommon after alloHSCT. There was a statistically significant association between the EBV and CMV oral shedding at C1 and the cumulative incidence of acute graft-versus-host disease (aGVHD). The results suggested that the presence of HSV-1 at C2 was related to a relapse. The HHV-7 oral shedding at C2 suggests a possible link between relapse, progression-free survival and overall survival of the patients. CONCLUSIONS: Patients who developed aGVHD showed higher CMV and EBV shedding in the oral cavity at aplasia, suggesting modifications to the pattern of immune cell response and inflammatory microenvironment.

Mishra, A., et al. (2021). "Objective and subjective physical function in allogeneic hematopoietic stem cell transplant recipients." Bone Marrow Transplant.

We conducted a prospective study of adult allogeneic hematopoietic cell transplantation (HCT) recipients to assess pre- and post-HCT physical function. Baseline measurements included a wrist actigraphy, a 6 min walk test (6MWT), an international physical activity questionnaire (IPAQ), and a Functional Assessment of Cancer Therapy-Bone Marrow Transplant (FACT-BMT) as well as serial post-HCT assessments of 6MWT, IPAQ, and FACT-BMT. Forty-seven patients were evaluable for functionality assessments, with a median follow-up of 54.5 months for surviving recipients. No patients demonstrated vigorous or very vigorous activity at any time during monitoring by wrist actigraphy; patients spent a median of 6 h daily sedentary. Self-reported activity via the IPAQ showed 36%, 43%, and 21% of subjects reporting light, moderate, and vigorous activity prior to HCT, respectively. Post-HCT 6MWTs on day +30 demonstrated the greatest association with subsequent survival and non-relapse mortality. A

decline in 6MWT distance over time also demonstrated worsened overall survival. This study shows the feasibility of fitness assessments and the ability to risk stratify for subsequent mortality, particularly using the 6MWT on the day +30 single time point assessment and change scores from baseline to day +30 post HCT. These pilot findings suggest important targets for future study.

Moreau, P., et al. (2021). "Maintenance with daratumumab or observation following treatment with bortezomib, thalidomide, and dexamethasone with or without daratumumab and autologous stem-cell transplant in patients with newly diagnosed multiple myeloma (CASSIOPEIA): an open-label, randomised, phase 3 trial." Lancet Oncol.

BACKGROUND: CASSIOPEIA part 1 showed superior depth of response and significantly improved progression-free survival with daratumumab, bortezomib, thalidomide, and dexamethasone (D-VTd) versus bortezomib, thalidomide, and dexamethasone (VTd) as induction and consolidation in patients with autologous stem-cell transplant (ASCT)-eligible newly diagnosed multiple myeloma. In part 2, we compared daratumumab maintenance versus observation only. METHODS: CASSIOPEIA is a two-part, open-label, randomised, phase 3 trial of patients aged 18-65 years with newly diagnosed multiple myeloma and Eastern Cooperative Oncology Group performance status 0-2, done in 111 European academic and community practice centres. In part 1, patients were randomly assigned (1:1) to induction and consolidation with D-VTd or VTd. Patients still on study who had a partial response or better were randomly assigned (1:1) by an interactive web-response system to daratumumab 16 mg/kg intravenously every 8 weeks (a reduced frequency compared with standard daratumumab long-term dosing) or observation only for up to 2 years. Stratification factors were induction treatment and depth of response in part 1. The part 2 primary endpoint was progression-free survival from second randomisation. This preplanned interim analysis of progression-free survival was done after 281 events and shall be considered the primary analysis of progression-free survival. Sponsor personnel and designees who were involved in the analysis were masked to treatment group until the independent data monitoring committee recommended that the preplanned interim analysis be considered the main analysis of progression-free survival in part 2. Otherwise, treatment assignments were unmasked. The interaction between induction and consolidation and maintenance was tested at a two-sided significance level of 0.05 by a stratified Cox regression model that included the interaction term between maintenance treatment and induction and consolidation treatment. Efficacy analyses were done in the maintenance-specific intention-to-treat population, which comprised all patients who underwent second randomisation. Safety was analysed in all patients in the daratumumab group who received at least one dose and all patients randomly assigned to observation only. This trial is registered with ClinicalTrials.gov, NCT02541383. Long-term follow-up is ongoing and the trial is closed to new participants. FINDINGS: Between May 30, 2016, and June 18, 2018, 886 patients (458 [84%] of 543 in the D-VTd group and 428 [79%] of 542 in the VTd group) were randomly assigned to daratumumab maintenance (n=442) or observation only (n=444). At a median follow-up of 35.4 months (IQR 30.2-39.9) from second randomisation, median progression-free survival was not reached (95% CI not evaluable [NE]-NE) with daratumumab versus 46.7 months (40.0-NE) with observation only (hazard ratio 0.53, 95% CI 0.42-0.68, p<0.0001). A prespecified analysis of progression-free survival results showed a significant interaction between maintenance and induction and consolidation therapy (p<0.0001). The most common grade 3 or 4 adverse events were lymphopenia (16 [4%] of 440 patients in the daratumumab group vs eight [2%] of 444 patients in the observation-only group), hypertension (13 [3%] vs seven [2%]), and neutropenia (nine [2%] vs ten [2%]). Serious adverse events occurred in 100 (23%) patients in the daratumumab group and 84 (19%) patients in the observation-only group. In the daratumumab group, two adverse events led to death (septic shock and natural killer-cell lymphoblastic lymphoma); both were related to treatment. INTERPRETATION: Daratumumab maintenance every 8 weeks for 2 years significantly reduced the risk of disease progression or death compared with observation only. Longer follow-up and other ongoing studies will shed further light on the optimal daratumumab-containing post-ASCT maintenance treatment strategy. FUNDING: Janssen Research & Development, the Intergroupe Francophone du Myelome, and the Dutch-Belgian Cooperative Trial Group for Hematology Oncology.

Morken, C., et al. (2021). "Barriers and facilitators to the use of survivorship care plans by hematopoietic stem cell transplant survivors and clinicians." Support Care Cancer.

PURPOSE: Survivors of hematopoietic stem cell transplants (HSCT) have complex care needs for the remainder of their lives, known as the survivorship period. Survivorship care plans (SCPs) have been proposed to improve care coordination and ultimately survivorship outcomes. We explored the barriers and facilitators of SCP use among HSCT survivors and their clinicians in order to develop more useful SCPs for the HSCT context. METHODS: Analogous surveys regarding perceived barriers to and facilitators of SCP use based on a sample SCP for a female allogenic

HSCT survivor were administered to HSCT survivors and non-transplant oncology and primary care clinicians. RESULTS: Twenty-seven HSCT survivors and 18 clinicians completed the survey. The main barriers to SCP use were lack of awareness of SCP existence, uncertainty regarding where to find SCP, unclear roles and responsibilities among healthcare teams, length of SCP, and difficultly understanding SCPs. The facilitators of SCP use were increased understanding of survivorship care needs, clarified roles and responsibilities of survivors and clinicians, SCPs that are readily available and searchable in electronic health record, increased awareness of SCP existence and provision to all survivors, and if the SCP is survivor-specific and up-to-date. CONCLUSIONS: Much of the work regarding SCPs has looked at barriers to creation and provision; however, our study examines factors influencing use of SCPs. By determining the barriers and facilitators surrounding SCP use for HSCT survivors and their clinicians, we can create SCP templates and clinical workflows to optimize SCP use, ideally leading to better outcomes for HSCT survivors.

Morton, S., et al. (2021). "Cytomegalovirus serological testing in potential allogeneic haematopoietic stem cell transplant recipients: A British Society for Haematology Good Practice Paper." Br J Haematol **195**(1): 73-75.

Murillo-Sanjuan, L., et al. (2021). "Post-hematopoietic stem cell transplant squamous cell carcinoma in patients with Fanconi anemia: a dreadful enemy." Clin Transl Oncol.

INTRODUCTION: Hematopoietic stem cell transplantation (HSCT) is a curative option for patients with Fanconi anemia (FA) and hematological manifestations but it does not prevent solid tumors, especially squamous cell carcinomas (SCC). METHODS: Retrospective study in 22 FA patients who had received HSCT and had been followed up beyond 2 years after HSCT. RESULTS: The median follow-up was 15 years. Six patients developed head-and-neck SCC after transplantation. The cumulative incidence of SCC at 15 and 30 years from the HSCT was 14.2% and 71.2%, respectively. One patient was diagnosed in stage IV and the rest, who were being followed up in cancer screening programs, in stage I. Treatment of SCC consisted of surgery in all patients; radiotherapy and chemotherapy were used in two patients and were poorly tolerated. CONCLUSION: FA patients have high risk of head-and-neck SCC. Multi-disciplinary programs for early cancer detection are of special relevance in these patients.

Myers, C. E., et al. (2021). "Using Whole Genome Sequences to Investigate Adenovirus Outbreaks in a Hematopoietic Stem Cell Transplant Unit." Front Microbiol **12**: 667790.

A recent surge in human mastadenovirus (HAdV) cases, including five deaths, amongst a haematopoietic stem cell transplant population led us to use whole genome sequencing (WGS) to investigate. We compared sequences from 37 patients collected over a 20-month period with sequences from GenBank and our own database of HAdVs. Maximum likelihood trees and pairwise differences were used to evaluate genotypic relationships, paired with the epidemiological data from routine infection prevention and control (IPC) records and hospital activity data. During this time period, two formal outbreaks had been declared by IPC, while WGS detected nine monophyletic clusters, seven were corroborated by epidemiological evidence and by comparison of single-nucleotide polymorphisms. One of the formal outbreaks was confirmed, and the other was not. Of the five HAdV-associated deaths, three were unlinked and the remaining two considered the source of transmission. Mixed infection was frequent (10%), providing a sentinel source of recombination and superinfection. Immunosuppressed patients harboring a high rate of HAdV positivity require comprehensive surveillance. As a consequence of these findings, HAdV WGS is being incorporated routinely into clinical practice to influence IPC policy contemporaneously.

Natvig, C., et al. (2021). "Association between employment status change and depression and anxiety in allogeneic stem cell transplant caregivers." J Cancer Surviv.

PURPOSE: Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is a demanding treatment that requires caregiver support during the first 100 days post-transplant. Little is known about the association between caregivers' employment changes and their well-being during this lengthy and challenging time when caregivers may be balancing work with caregiving responsibilities. METHODS: We used data from employed caregivers of Allo-HSCT patients who participated in two randomized clinical trials (N = 187) of an intervention for caregivers. Caregiver depression and anxiety were assessed using the Center for Epidemiologic Studies Depression and the Spielberger State-Trait Anxiety Inventory. ANCOVA was used to measure the associations between reducing work with depression and anxiety. Caregiver's demographics and baseline employment status were controlled in the analysis along with the patient's transplant conditioning intensity. RESULTS: Approximately 45% of caregivers reduced hours worked following the resumption of their caregiving duties. These caregivers, on average, had 3.49 points higher depression scores than caregivers who did not report a reduction in work ($p < 0.01$). Similarly, these caregivers also reported, on average, 3.56 higher

anxiety scores ($p < 0.10$). CONCLUSIONS: Caregivers who reduced hours worked while caregiving reported greater distress. The underlying cause of this distress deserves further investigation. IMPLICATIONS FOR CANCER SURVIVORS: Caregivers of patients diagnosed with cancer may experience considerable stress related to work discontinuation and caregiving. Interventions are needed to support caregivers who are trying to balance work and caregiving responsibilities.

Obeid, K. M., et al. (2021). "Early Clostridioides difficile infection characterizations, risks, and outcomes in allogeneic hematopoietic stem cell and solid organ transplant recipients." Transpl Infect Dis: e13720.

BACKGROUND: Clostridioides difficile infection (CDI) frequently complicates allogeneic hematopoietic stem cell (allo-HCT) and solid organ transplantation (SOT). METHODS: We retrospectively analyzed risk factors and outcomes of CDI occurring within 30 days of transplant. RESULTS: Between March 2010 and June 2015, 466 allo-HCT and 1454 SOT were performed. The CDI cumulative incidence (95% CI) was 10% (8-13) and 4% (3-5), following allo-HCT and SOT, respectively ($p < .01$), occurring at a median (range) 7.5 days (1-30) and 11 (1-30), respectively ($p = .18$). In multivariate analysis, fluoroquinolones use within 14 days pre-transplantation was a risk factor for CDI following allo-HCT (HR 4.06 [95% CI 1.31-12.63], $p = .02$), and thoracic organ(s) transplantation was a risk factor for CDI following SOT (HR 3.03 [95% CI 1.31-6.98]) for lung and 3.90 (1.58-9.63) for heart and heart/kidney transplant, $p = .02$. Compared with no-CDI patients, the length of stay (LOS) was prolonged in both allo-HCT (35 days [19-141] vs. 29 [13-164], $p < .01$) and SOT with CDI (16.5 [4-101] vs. 7 [0-159], $p < .01$), though not directly attributed to CDI. In allo-HCT, severe acute graft-versus-host disease (aGVHD) occurred more frequently in patients with CDI (33.3% vs. 15.8% without CDI, $p = .01$) and most aGVHD (87.5%) followed CDI. Non-relapse mortality or overall survival, not attributed to CDI, were also similar in both allo-HCT and SOT. CONCLUSIONS: Early post-transplant CDI is frequent, associated with fluoroquinolones use in allo-HCT and the transplanted organ in SOT, and is associated with longer LOS in both the groups without difference in survival but with increased aGVHD in allo-HCT.

Ombres, R., et al. (2021). "Serial frailty assessments following allogeneic stem cell transplant in older adults: A pilot study." J Geriatr Oncol.

INTRODUCTION: Increasing numbers of older adults undergo allogeneic stem cell transplantation (SCT) as the only chance of meaningful survival for hematologic malignancies. However, toxicities in vulnerable patients may offset the benefits of SCT. Frailty and abnormal geriatric assessment (GA) prior to SCT have been associated with decreased overall survival in persons aged 60 and older. The purpose of this pilot study was to determine the prevalence of baseline GA deficits and frailty, the prevalence of frailty or death at three and six months after allogeneic SCT, and associations between baseline assessments and the presence of frailty or death post-SCT. METHODS: We enrolled 50 patients aged 60 years and older and completed a baseline GA including comorbidity, polypharmacy, nutrition, physical performance, functional status, social support, depression and anxiety, and cognition. Frailty was defined as three or more abnormalities of gait speed, grip strength, weight loss, physical activity, and exhaustion, and was assessed at baseline, three months, and six months after SCT. A composite outcome of frailty or death at three months and six months was analyzed. RESULTS: Frailty was present in 11/50 (22%) of patients at baseline. Ten patients did not complete three- month follow-up, and twelve patients did not complete six-month follow-up. Of those with follow-up data, 22 patients (55%) were frail or deceased three months after SCT, and 27 patients (71%) were frail or deceased six months after SCT. Frailty at baseline was not significantly associated with frailty or death at three or six months after SCT. However, the study's small enrollment limits conclusions on these associations. CONCLUSION: GA deficits and frailty are prevalent in older adult SCT recipients at baseline and after transplant. Future studies should aim for larger enrollment in order to validate associations between these deficits and outcomes, especially survival, functional status, and quality of life following SCT.

Patel, P., et al. (2021). "Clinical practice guideline for the prevention of oral and oropharyngeal mucositis in pediatric cancer and hematopoietic stem cell transplant patients: 2021 update." Eur J Cancer **154**: 92-101.

PURPOSE: To update the 2015 clinical practice guideline for the prevention of oral mucositis in pediatric cancer or hematopoietic stem cell transplant (HSCT) patients. METHODS: We performed seven systematic reviews of mucositis prevention. Three reviews included randomized controlled trials (RCTs) conducted in pediatric and adult patients evaluating cryotherapy, keratinocyte growth factor (KGF) or photobiomodulation therapy with a focus on efficacy. Three reviews included studies of any design conducted in pediatric patients evaluating these same interventions with a focus on adverse events and feasibility. One review included all RCTs of any intervention for mucositis prevention in pediatric patients. Primary outcome was severe oral mucositis. RESULTS: We included 107 unique studies of cryotherapy (22 RCTs and 4 pediatric studies); KGF

(15 RCTs and 12 pediatric studies); photobiomodulation therapy (29 RCTs and 8 pediatric studies) and any intervention (31 pediatric RCTs). Effects on severe mucositis reduction from RCTs were cryotherapy risk ratio (RR) 0.49 and 95% confidence interval (CI) 0.31-0.76; palifermin RR 0.81 and 95% CI 0.69-0.95 and photobiomodulation therapy RR 0.40 and 95% CI 0.27-0.60. Cryotherapy was not feasible in young children while photobiomodulation therapy was feasible across age groups. Palifermin was associated with adverse effects. CONCLUSIONS: Cryotherapy should be used for older cooperative pediatric patients who will receive short infusions of melphalan or 5-fluorouracil. Intraoral photobiomodulation therapy (620-750 nm spectrum) should be used in pediatric patients undergoing autologous or allogeneic HSCT and for pediatric head and neck carcinoma patients undergoing radiotherapy. Palifermin should not be used routinely in pediatric cancer or HSCT patients.

Patel, R., et al. (2021). "Black multiple myeloma patients undergoing upfront autologous stem cell transplant have similar survival outcomes compared to whites: a propensity-score matched analysis." Am J Hematol.

Peric, Z., et al. (2021). "Influence of pretransplant inflammatory bowel disease on the outcome of allogeneic hematopoietic stem cell transplantation: a matched-pair analysis study from the Transplant Complications Working Party (TCWP) of the EBMT." Bone Marrow Transplant.

Pirotte, M., et al. (2021). "Erythroferrone and hepcidin as mediators between erythropoiesis and iron metabolism during allogeneic hematopoietic stem cell transplant." Am J Hematol **96**(10): 1275-1286.

Hematopoietic cell transplantation (HCT) brings important alterations in erythropoiesis and iron metabolism. Hepcidin, which regulates iron metabolism, increases in iron overload or inflammation and decreases with iron deficiency or activated erythropoiesis. Erythroferrone (ERFE) is the erythroid regulator of hepcidin. We investigated erythropoiesis and iron metabolism after allogeneic HCT in 70 patients randomized between erythropoietin (EPO) treatment or no EPO, by serially measuring hepcidin, ERFE, CRP (inflammation), soluble transferrin receptor (sTfR, erythropoiesis), serum iron and transferrin saturation (Tsat; iron for erythropoiesis) and ferritin (iron stores). We identified biological and clinical factors associated with serum hepcidin and ERFE levels. Serum ERFE correlated overall with sTfR and reticulocytes and inversely with hepcidin. Erythroferrone paralleled sTfR levels, dropping during conditioning and recovering with engraftment. Inversely, hepcidin peaked after conditioning and decreased during engraftment. Erythroferrone and hepcidin were not significantly different with or without EPO. Multivariate analyses showed that the major determinant of ERFE was erythropoiesis (sTfR, reticulocytes or serum Epo). Pretransplant hepcidin was associated with previous RBC transfusions and ferritin. After transplantation, the major determinants of hepcidin were iron status (ferritin at all time points and Tsat at day 56) and erythropoiesis (sTfR or reticulocytes or ERFE), while the impact of inflammation was less clear and clinical parameters had no detectable influence. Hepcidin remained significantly higher in patients with high compared to low pretransplant ferritin. After allogeneic HCT with or without EPO therapy, significant alterations of hepcidin occur between pretransplant and day 180, in correlation with iron status and inversely with erythroid ERFE.

Pochon, C., et al. (2021). "Improved outcome in children compared to adolescents and young adults after allogeneic hematopoietic stem cell transplant for acute myeloid leukemia: a retrospective study from the Francophone Society of Bone Marrow Transplantation and Cell Therapy (SFGM-TC)." J Cancer Res Clin Oncol.

BACKGROUND: There are currently few data on the outcome of acute myeloid leukemia (AML) in adolescents after allogeneic HSCT. The aim of this study is to describe the outcome and its specific risk factors for children, adolescents and young adults after a first allogeneic HSCT for AML. METHODS: In this retrospective study, we compared the outcome of AML patients receiving a first allogeneic HSCT between 2005 and 2017 according to their age at transplantation's time: children (< 15 years, n = 564), adolescent and post-adolescent (APA) patients (15-25 years, n = 647) and young adults (26-40 years; n = 1434). RESULTS: With a median follow-up of 4.37 years (min-max 0.18-14.73 years), the probability of 2-year overall survival (OS) was 71.4% in children, 61.1% in APA patients and 62.9% in young adults (p = 0.0009 for intergroup difference). Both relapse and non-relapse mortality (NRM) Cumulative Incidence (CI) estimated at 2 years were different between the age groups (30.8% for children, 35.2% for APA patients and 29.4% for young adults-p = 0.0254, and 7.0% for children, 10.6% for APA patients and 14.2% for young adults, p < 0.0001; respectively). Whilst there was no difference between the three groups for grade I to IV acute GVHD CI at 3 months, the chronic GVHD CI at 2 years was higher in APA patients and young adults (31.4% and 36.4%, respectively) in comparison to the children (17.5%) (p < 0.0001). In multivariable analysis, factors associated with death were AML cytogenetics (HR1.73 [1.29-2.32] for intermediate risk 1, HR 1.50 [1.13-2.01] for intermediate risk 2, HR 2.22 [1.70-2.89] for high cytogenetics risk compared to low risk), use of TBI >/=

8 Grays (HR 1.33 [1.09-1.61]), disease status at transplant (HR 1.40 [1.10-1.78] for second Complete Remission (CR), HR 2.26 [1.02-4.98] for third CR and HR 3.07 [2.44-3.85] for active disease, compared to first CR), graft source (HR 1.26 [1.05-1.50] for Peripheral Blood Stem Cells compared to Bone Marrow) and donor age (HR 1.01 (1-1.02] by increase of 1 year). CONCLUSION: Age is an independent risk factor for NRM and extensive chronic GVHD. This study suggests that APA patients with AML could be beneficially treated with a chemotherapy-based MAC regimen and bone marrow as a stem cells source.

Pravin, R. R., et al. (2021). "Mortality Trends of Oncology and Hematopoietic Stem Cell Transplant Patients Supported on Extracorporeal Membrane Oxygenation: A Systematic Review and Meta-Analysis." J Intensive Care Med: 8850666211021561.

BACKGROUND: There is an increasing frequency of oncology and hematopoietic stem cell transplant (HSCT) patients seen in the intensive care unit and requiring extracorporeal membrane oxygenation (ECMO), however, prognosis of this population over time is unclear. METHODS: MEDLINE, EMBASE, Cochrane and Web of Science were searched from earliest publication until April 10, 2020 for studies to determine the mortality trend over time in oncology and HSCT patients requiring ECMO. Primary outcome was hospital mortality. Random-effects meta-analysis model was used to obtain pooled estimates of mortality and 95% confidence intervals. A priori subgroup metanalysis compared adult versus pediatric, oncology versus HSCT, hematological malignancy versus solid tumor, allogeneic versus autologous HSCT, and veno-arterial versus veno-venous ECMO populations. Multivariable meta-regression was also performed for hospital mortality to account for year of study and HSCT population. RESULTS: 17 eligible observational studies (n = 1109 patients) were included. Overall pooled hospital mortality was 72% (95% CI: 65, 78). In the subgroup analysis, only HSCT was associated with a higher hospital mortality compared to oncology subgroup [84% (95% CI: 70, 93) vs. 66% (95% CI: 56, 74); P = 0.021]. Meta-regression showed that HSCT was associated with increased mortality [adjusted odds ratio (aOR) 3.84 (95% CI 1.77, 8.31)], however, mortality improved with time [aOR 0.92 (95% CI: 0.85, 0.99) with each advancing year]. CONCLUSION: This study reports a high overall hospital mortality in oncology and HSCT patients on ECMO which improved over time. The presence of HSCT portends almost a 4-fold increased risk of mortality and this finding may need to be taken into consideration during patient selection for ECMO.

Rahi, M. S., et al. (2021). "Fungal infections in hematopoietic stem-cell transplant patients: a review of epidemiology, diagnosis, and management." Ther Adv Infect Dis **8**: 20499361211039050.

The advent of bone marrow transplant has opened doors to a different approach and offered a new treatment modality for various hematopoietic stem-cell-related disorders. Since the first bone marrow transplant in 1957, there has been significant progress in managing patients who undergo bone marrow transplants. Plasma-cell disorders, lymphoproliferative disorders, and myelodysplastic syndrome are the most common indications for hematopoietic stem-cell transplant. Despite the advances, invasive fungal infections remain a significant cause of morbidity and mortality in this high-risk population. The overall incidence of invasive fungal infection in patients with hematopoietic stem-cell transplant is around 4%, but the mortality in patients with allogeneic stem-cell transplant is as high as 13% in one study. Type of stem-cell transplant, conditioning regimen, and development of graft-versus-host disease are some of the risk factors that impact the risk and outcomes in patients with invasive fungal infections. Aspergillus and candida remain the two most common organisms causing invasive fungal infections. Molecular diagnostic methods have replaced some traditional methods due to their simplicity of use and rapid turnaround time. Primary prophylaxis has undoubtedly shown to improve outcomes even though breakthrough infection rates remain high. The directed treatment has seen a significant shift from amphotericin B to itraconazole, voriconazole, and echinocandins, which have shown better efficacy and fewer adverse effects. In this comprehensive review, we aim to detail epidemiology, risk factors, diagnosis, and management, including prophylaxis, empiric and directed management of invasive fungal infections in patients with hematopoietic stem-cell transplant.

Rastogi, N., et al. (2021). "Successful Allogeneic Hematopoietic Stem Cell Transplant for CARMIL2 Deficiency." J Pediatr Hematol Oncol.

Revels, J. W., et al. (2021). "Imaging features of fungal pneumonia in haematopoietic stem cell transplant patients." Pol J Radiol **86**: e335-e343.

Patients who have received haematopoietic stem cell transplantation (HSCT) have a high rate of pulmonary complications, and in this immunosuppressed population, fungal pneumonia is of great concern. Fungal pneumonia can have a similar appearance to non-infectious pulmonary processes in HSCT patients, and radiologists should be familiar with the subtle features that may help to differentiate these disease entities. The focus of this article is on the diagnosis of fungal pneumonia in HSCT patients with an emphasis on radiologists' roles in establishing the diagnosis of fungal pneumonia and the guidance of clinical management.

Richards, H., et al. (2021). "Salvage second autologous stem cell transplant for relapsed multiple myeloma in the novel agent era benefits a subset of patients: single-center UK experience." Leuk Lymphoma: 1-4.

Rocha, V., et al. (2021). "Impact of mother donor, peripheral blood stem cells and measurable residual disease on outcomes after haploidentical hematopoietic cell transplantation with post-transplant cyclophosphamide in children with acute leukaemia." Bone Marrow Transplant.

Haploidentical hematopoietic-cell transplantation using post-transplant cyclophosphamide(Haplo-PTCy) is a feasible procedure in children with haematologic malignancies. However, data of a large series of children with acute leukaemia(AL) in this setting is missing. We analysed 144 AL Haplo-PTCy paediatric recipients; median age was 10 years. Patients had acute lymphoblastic(ALL; n = 86) or myeloblastic leukaemia(AML; n = 58) and were transplanted in remission(CR1: n = 40; CR2: n = 57; CR3+: n = 27) or relapse (n = 20). Bone marrow was the graft source in 57%; donors were father (54%), mother (35%), or sibling (11%). Myeloablative conditioning was used in 87%. Median follow-up was 31 months. At day +100, cumulative incidence (CI) of neutrophil recovery and acute GVHD (II-IV) were 94% and 40%, respectively. At 2-years, CI of chronic GVHD and relapse, were 31%, 40%, and estimated 2-year overall survival (OS), leukaemia-free survival (LFS) and graft-versus-host-relapse-free survival (GRFS) were 52%, 44% and 34% respectively. For patients transplanted in remission, positive measurable residual disease (MRD) prior to transplant was associated with decreased LFS (p = 0.05) and GRFS (p = 0.003) and increased risk of relapse (p = 0.02). Mother donor was associated with increased risk of chronic GVHD (p = 0.001), decreased OS (p = 0.03) and GRFS (p = 0.004). Use of PBSC was associated with increased risk of chronic GVHD (p = 0.04). In conclusion, achieving MRD negativity pre-transplant, avoiding use of mother donors and PBSC as graft source may improve outcomes of Haplo-PTCy in children with AL.

Rodriguez Feria, D., et al. (2021). "Membranous Glomerulopathy After Autologous Hematopoietic Stem Cell Transplant in a Patient With Multiple Myeloma." Kidney Int Rep **6**(8): 2243-2245.

Ruhayel, S. D., et al. (2021). "Viridans Group Streptococci in Pediatric Leukemia and Stem Cell Transplant: Review of a Risk-stratified Guideline for Empiric Vancomycin in Febrile Neutropenia." Pediatr Infect Dis J **40**(9): 832-834.

Viridans group streptococci (VGS) are an important cause of sepsis in immunosuppressed children. We reviewed the effectiveness of risk-stratified addition of vancomycin to empiric febrile neutropenia therapy among 107 children with leukemia or undergoing an allogeneic transplant. Of 19 VGS bacteremia episodes, 78.9% were susceptible to risk-stratified antibiotics including 100% from high-risk patients. All blood cultures were flagged positive within 24 hours.

Sahasrabudhe, S. A., et al. (2021). "Population Pharmacokinetic Analysis of N-Acetylcysteine in Pediatric Patients With Inherited Metabolic Disorders Undergoing Hematopoietic Stem Cell Transplant." J Clin Pharmacol.

N-acetylcysteine (NAC) has been used in patients with cerebral adrenoleukodystrophy as an antioxidant agent in association with hematopoietic stem cell transplant (HSCT). However, an understanding of the pharmacokinetic characteristics of intravenous NAC dosing in these patients is limited. If and how NAC pharmacokinetics change following the transplant is unknown. Toward that end, a total of 260 blood samples obtained from 18 pediatric patients with inherited metabolic disorders who underwent HSCT were included in a population pharmacokinetic analysis using nonlinear mixed-effects modeling. NAC clearance (CL) and volume of distribution (V) were explored on 3 occasions: -7, +7, and +21 days relative to transplant. Additionally, the effect of transplant procedure on NAC disposition was explored by accounting for between-occasion variability. The covariate OCC was modeled as a fixed-effect parameter on CL and/or V1. A 2-compartment model adequately described the pharmacokinetics of total NAC. Weight-based allometric scaling on pharmacokinetic parameters was assumed using standard coefficients. Estimates for CL, central (V1), and peripheral volume (V2), and intercompartment clearance were 14.7 L/h, 23.2 L, 17.1 L, 3.99 L/h, respectively, for a 70-kg person. The data only supported between-subject variability in CL (12%) and V1 (41%). Residual variability was estimated to be 16%. HSCT did not change CL and V1 significantly, and analysis across occasions did not reveal any trends. Pharmacokinetic parameter estimates were in general comparable to those reported previously in different populations. These results suggest that dosing of NAC does not need to be altered following HSCT.

Shah, N., et al. (2021). "Improved outcome in AML relapse after allogeneic transplant with high-intensity chemotherapy followed by 2nd allogeneic stem cell transplant or donor lymphocyte infusion." Ann Hematol **100**(10): 2585-2592.

Acute myeloid leukemia (AML) relapse after allogeneic stem cell transplant (alloSCT) remains a major therapeutic challenge. While patients with longer remission after initial alloSCT are recommended to receive cell therapy (CT) such as 2(nd)alloSCT or

donor lymphocyte infusion (DLI), survival for patients who relapse within 6 months of alloSCT has been dismal. We evaluated the outcomes of AML relapse after alloSCT to assess the impact of different treatments on long-term survival. One hundred and seventy-two patients with AML underwent alloSCT at the Penn State Cancer Institute from January 2014 to August 2019. Sixty-nine patients relapsed (median age, 60 years; range, 10-75). Of these, 4 patients underwent 2(nd)alloSCT, and 26 received DLI. One-year overall survival (OS) in all cases was 20.3% (95% CI: 11.8-30.4%). Patients with ECOG performance status (PS) 0-2 at relapse showed a better 1-year OS than those with PS 3-4. Median OS for patients who received chemotherapy only or chemotherapy with CT was 74 or 173.5 days, respectively ($p < 0.001$). Relapsed patients receiving conventional re-induction chemotherapy were categorized as the high-intensity chemotherapy (H) group, while those receiving treatments such as hypomethylating agents or targeted agents were categorized as the low-intensity chemotherapy (L) group. The H group showed a better 1-year OS compared with the L group. Patients who received H + CT showed a better 1-year OS of 52.9% than the other 3 groups ($p < 0.001$). Even for patients with post-alloSCT remission duration of less than 6 months, the statistical significance was preserved. Factors including age, donor source at 1(st)alloSCT, time to relapse, blast counts, PS at relapse, and treatment type after post-alloSCT relapse were used for a multivariate analysis, and matched or mismatched related donor and H + CT after alloSCT were identified as independent factors associated with OS. These findings support the use of H + CT as the treatment option of choice for AML patients who relapse after alloSCT when feasible.

Shanthikumar, S., et al. (2021). "Pulmonary surveillance in pediatric hematopoietic stem cell transplant: A multinational multidisciplinary survey." Cancer Rep (Hoboken): e1501.

BACKGROUND: Hematopoietic Stem Cell Transplant (HSCT) is an established treatment for malignant and non-malignant conditions and pulmonary disease is a leading cause of late term morbidity and mortality. Accurate and early detection of pulmonary complications is a critical step in improving long term outcomes. Existing guidelines for surveillance of pulmonary complications post-HSCT contain conflicting recommendations. AIM: To determine the breadth of current practice in monitoring for pulmonary complications of pediatric HSCT. METHODS: An institutional review board approved, online, anonymous multiple-choice survey was distributed to HSCT and pulmonary physicians from the United States of America and Australasia using the REDcap platform. The survey was developed by members of the American Thoracic Society Working Group on Complications of Childhood Cancer, and was designed to assess patient management and service design. RESULTS: A total of 40 (34.8%) responses were received. The majority (62.5%) were pulmonologists, and 82.5% were from the United States of America. In all, 67.5% reported having a protocol for monitoring pulmonary complications and 50.0% reported adhering "well" or "very well" to protocols. Pulmonary function tests (PFTs) most commonly involved spirometry and diffusion capacity for carbon monoxide. The frequency of PFTs varied depending on time post-HSCT and presence of complications. In all, 55.0% reported a set threshold for a clinically significant change in PFT. CONCLUSIONS: These results illustrate current variation in surveillance for pulmonary complications of pediatric HSCT. The results of this survey will inform development of future guidelines for monitoring of pulmonary complications after pediatric HSCT.

Sharma, S. K., et al. (2021). "Myeloablative Versus Reduced Intensity Conditioning Regimens for Allogeneic Hematopoietic Stem Cell Transplant for Acute Myeloid Leukemia and Myelodysplastic Syndrome: A Retrospective Analysis." Indian J Hematol Blood Transfus **37**(3): 472-478.

The conditioning regimens used for the allo-HSCT include either myeloablative conditioning (MAC) or reduced intensity conditioning (RIC) regimens based on the age, performance status and co-morbidities. Studies comparing the survival outcomes of RIC and MAC allo-HSCT in AML and MDS patients have reported contradictory results. We therefore retrospectively analyzed our data of AML and MDS patients who received MAC and RIC allo-HSCT at our center and compared the long term outcome of the two conditioning regimens. One hundred twenty six consecutive patients were evaluated, 32 (25.4%) underwent MAC allo-HSCT and 94 (74.6%) underwent RIC allo-HSCT. The most common MAC regimen used was busulfan plus cyclophosphamide and the most common RIC regimen used was fludarabine plus melphalan. The median age was higher in RIC group (44 years, range 4-75 years) compared to MAC group (31 yrs, range 6-51 yrs, $p = 0.001$). There was no significant difference in terms of overall survival ($p = 0.498$), relapse-free survival ($p = 0.791$) and non-relapse mortality ($p = 0.366$) between the two groups. In multivariate analysis, only chronic graft-versus-host disease resulted in decreased risk of relapse and improved overall survival irrespective of the conditioning regimens used.

Stadtmauer, E. A., et al. (2021). "Adjuvanted recombinant zoster vaccine in adult autologous stem cell transplant recipients: polyfunctional immune

responses and lessons for clinical practice." Hum Vaccin Immunother: 1-11.

Immunocompromised individuals, particularly autologous hematopoietic stem cell transplant (auHSCT) recipients, are at high risk for herpes zoster (HZ). We provide an in-depth description of humoral and cell-mediated immune (CMI) responses by age (protocol-defined) or underlying disease (post-hoc) as well as efficacy by underlying disease (post-hoc) of the adjuvanted recombinant zoster vaccine (RZV) in a randomized observer-blind phase III trial (ZOE-HSCT, NCT01610414). 1846 adult auHSCT recipients were randomized to receive a first dose of either RZV or placebo 50-70 days post-auHSCT, followed by the second dose at 1-2 months (M) later. In cohorts of 114-1721 participants, at 1 M post-second vaccine dose: Anti-gE antibody geometric mean concentrations (GMCs) and median gE-specific CD4[2+] T-cell frequencies (CD4 T cells expressing >/=2 of four assessed activation markers) were similar between 18-49 and >/=50-year-olds. Despite lower anti-gE antibody GMCs in non-Hodgkin B-cell lymphoma (NHBCL) patients, CD4[2+] T-cell frequencies were similar between NHBCL and other underlying diseases. The proportion of polyfunctional CD4 T cells increased over time, accounting for 79.6% of gE-specific CD4 T cells at 24 M post-dose two. Vaccine efficacy against HZ ranged between 42.5% and 82.5% across underlying diseases and was statistically significant in NHBCL and multiple myeloma patients. In conclusion, two RZV doses administered early post-auHSCT induced robust, persistent, and polyfunctional gE-specific immune responses. Efficacy against HZ was also high in NHBCL patients despite the lower humoral response.

PLAIN LANGUAGE SUMMARYWhat is the context?After haematopoletic stem cell transplantation, patlents have impaired immunity from conditioning chemotherapy regimens, often exacerbated by underlying diseases, putting them at high risk of developing herpes zoster. In this population, antiviral prophylaxis is the current standard of care to reduce herpes zoster risk. Vaccination provides an additional means to prevent herpes zoster. Live-attenuated vaccines are generally contraindicated in immuonocompromised patients. A non-live, adjuvanted recombinant zoster vaccine (RZV, Shingrix, GSK), has been approved for use in adults 250 years of age in the European Union, United States, Canada, Australia, Japan, and China. This vaccine is highly efficacious at preventing herpes zoster in adults over 50 years of age, as demonstrated in large, placebo-controlled randomised trials. Importantly, Shingrix use is not contraindicated in immunocompromised conditions, and was found to be highly efficacious in adults who had recently undergone autologous haematopoleticstem cell transplant.What is new?In autologous haematopoietic stem cell transplant recipients in whom Shingrix has demonstrated efficacy, two doseselicited high and persistent immune responses. Date presented here further support our understanding of the impact of specific factors such as age or underlying diseases on the vaccine's effect in the population studies, as well as the characteristics of the elicited cell-mediated immune responses.What is the impact?These results indicate that Shingrix, given shortly after haematopoletic stem cell transplant, can induce robust immune responses and reduce the risk of herpes zoster, even in individuals with immunosuppression due to underlying disease and/or use of immunosuppressive therapies, regardless of age or underlying disease.

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Stajner, T., et al. (2021). "Risk of reactivated toxoplasmosis in haematopoietic stem cell transplant recipients: a prospective cohort study in a setting withholding prophylaxis." Clin Microbiol Infect.

OBJECTIVES: Reactivation of latent toxoplasmosis may be life-threatening in haematopoietic stem cell transplant (HSCT) recipients. We conducted an eight-year-long prospective study on the diagnosis and monitoring of reactivated toxoplasmosis in paediatric HSCT recipients. The primary objective was to determine the incidence of reactivated toxoplasmosis in a setting that withholds prophylaxis until engraftment. The second objective was to identify the subgroups of HSCT recipients particularly prone to reactivation who may benefit the most from regular PCR follow-up. METHODS: Serological and qPCR screening targeting the Toxoplasma 529 bp gene was performed pre-HSCT, and continued by weekly monitoring post-HSCT for a median time of 104 days. RESULTS: Reactivated toxoplasmosis was diagnosed in 21/104 (20.2%), predominantly in allo- (19/75) and rarely in auto-HSCT (2/29) recipients. Over 50% (14/21) of cases were diagnosed during the first month post-HSCT, while awaiting engraftment without prophylaxis. Toxoplasma disease evolved in only three (14.3%, 3/21) patients, all treated by allo-HSCT. Reactivation was more frequent in patients treated for acute lymphoblastic leukaemia (3/27, p=0.03) and especially, in recipients of haploidentical stem cells (10/20, p=0.005). Seronegative status of the donor (where was known) contributed to 75% (12/16) cases of reactivated toxoplasmosis after allo-HSCT. CONCLUSIONS: The presented results show that peripheral blood-based qPCR, both pre- and post-HSCT, is a valuable asset for the diagnosis of reactivated toxoplasmosis, whereas the results of serology in recipients should be interpreted with caution. Weekly qPCR monitoring, at least until successful engraftment and administration of

prophylaxis, allows for prompt introduction of specific treatment.

Straka, C., et al. (2021). "Full or intensity-reduced high-dose melphalan and single or double autologous stem cell transplant with or without bortezomib consolidation in patients with newly diagnosed multiple myeloma." Eur J Haematol.

OBJECTIVE: A post hoc subgroup analysis of two phase III trials (NCT00416273, NCT00416208) was carried out to investigate the influence of 100/140 and 200 mg/m(2) melphalan as well as single/double autologous stem cell transplantation (ASCT) on progression-free survival (PFS). Additionally, the effect of bortezomib consolidation on PFS was analyzed. METHODS: Following induction therapy and high-dose melphalan with subsequent ASCT, patients with newly diagnosed multiple myeloma (NDMM) were randomized 1:1 to either four 35-day cycles of bortezomib consolidation (1.6 mg/m(2) IV on days 1, 8, 15, 22) or observation. RESULTS: Of the 340 patients included in this analysis, 13.5% received 1 x MEL100/140, 22.9% 2 x MEL100/140, 31.2% 1 x MEL200, and 32.4% 2 x MEL200. With higher cumulative melphalan dose, PFS improved (P = .0085). PFS curves of patients treated with 2 x MEL100/140 and 1 x MEL200 were very similar. The superior dose effect of MEL200 over MEL100/140 was non-existent in the bortezomib consolidation arm but pronounced in the observation arm (P = .0015). Similarly, double ASCT was only beneficial in patients without bortezomib consolidation (P = .0569). CONCLUSIONS: Full dose melphalan and double transplantation seem advantageous only as long as patients are not receiving bortezomib consolidation afterwards.

Tanaka, T. D., et al. (2021). "Successful treatment of pulmonary hypertension following hematopoietic stem cell transplant with a single oral tadalafil: a case report." Pulm Circ **11**(3): 20458940211027791.

A 46-year-old man who had undergone hematopoietic stem cell transplant twice because of acute lymphoblastic leukemia with recurrence presented with dyspnea, leading to a diagnosis of pulmonary arterial hypertension which was quickly and effectively treated with the phosphodiesterase type 5 inhibitor tadalafil. To our knowledge, pulmonary arterial hypertension related to hematologic malignancies requiring hematopoietic stem cell transplant is rarely reported. Importantly, the present case suggests that early diagnosis and treatment with a pulmonary vasodilator, such as tadalafil, can greatly decrease pulmonary vascular resistance in patients with severe pulmonary arterial hypertension after hematopoietic stem cell transplant and can then improve other symptoms. Accordingly, pulmonary vascular disease should be considered if respiratory symptoms develop following hematopoietic stem cell transplant, because treatment with pulmonary vasodilator may lead to significant improvement in pulmonary arterial hypertension.

Teixeira, G. M., et al. (2021). "Applicability of the acute leukemia (AL) - EBMT score as a prognostic model for allogeneic hematopoietic stem cell transplantation: a single-center, prospective, cohort study at a reference transplant center in Brazil." Hematol Transfus Cell Ther.

INTRODUCTION: The Acute Leukemia-European Society for Blood and Marrow Transplantation (AL-EBMT) risk score was recently developed and validated by Shouval et al. OBJECTIVE: To assess the ability of this score in predicting the 2-year overall survival (OS-2), leukemia-free survival (LFS-2) and transplant-related mortality (TRM) in acute leukemia (AL) adult patients undergoing a first allogeneic hematopoietic stem cell transplant (HSCT) at a transplant center in Brazil. METHODS: In this prospective, cohort study, we used the formula published by Shouval et al. to calculate the AL-EBMT score and stratify patients into three risk categories. RESULTS: A total of 79 patients transplanted between 2008 and 2018 were analyzed. The median age was 38 years. Acute myeloid leukemia was the most common diagnosis (68%). Almost a quarter of the cases were at an advanced stage. All hematopoietic stem cell transplantations (HSCTs) were human leukocyte antigen-matched (HLA-matched) and the majority used familial donors (77%). Myeloablative conditioning was used in 92% of the cases. Stratification according to the AL-EBMT score into low-, intermediate- and high-risk groups yielded the following results: 40%, 12% and 47% of the cases, respectively. The high scoring group was associated with a hazard ratio of 2.1 (p = 0.007), 2.1 (p = 0.009) and 2.47 (p = 0.01) for the 2-year OS, LFS and TRM, respectively. CONCLUSION: This study supports the ability of the AL-EBMT score to reasonably predict the 2-year post-transplant OS, LFS and TRM and to discriminate between risk categories in adult patients with AL, thus confirming its usefulness in clinical decision-making in this setting. Larger, multicenter studies may further help confirm these findings.

Tschernia, N. P., et al. (2021). "Safety and efficacy of pembrolizumab prior to allogeneic stem cell transplant in Acute Myeloid Leukemia." Transplant Cell Ther.

BACKGROUND: Programmed death-1 (PD-1) is an integral component of acute myeloid leukemia (AML) immune evasion, chemotherapy resistance, and disease progression. PD-1 inhibitors are being investigated as treatment for AML in combination with hypomethylating agents and cytotoxic chemotherapy with encouraging findings. OBJECTIVE: Although allogeneic stem cell transplant (alloSCT) remains the

most established curative treatment for relapsed and refractory AML patients in complete remission, there are limited data on the clinical outcomes and safety of immune checkpoint inhibitors (ICIs) prior to alloSCT in AML. STUDY DESIGN: We compared clinical outcomes of AML patients receiving high-dose cytarabine followed by pembrolizumab (n=8) in a phase II clinical trial (NCT02768792) prior to alloSCT versus a historical control group of AML patients who received alloSCT without prior ICI exposure (n=18). The nonparametric Jonckheere-Terpstra test was used to test for a difference in the ordered severity categories of aGVHD within 100 days of transplant. The time-to-event estimates for OS and relapse-free survival were calculated using the Kaplan-Meier method and compared using a log rank test. RESULTS: One-year survival was not significantly different between both treatment groups (67% versus 78%, p=0.34). 100-day mortality was 0% in the pembrolizumab cohort versus 17% in control group, and there was no increase in grade III-IV acute graft-versus-host disease in patients treated with pembrolizumab prior to alloSCT. No chronic graft-versus-host disease was seen in patients treated with pembrolizumab prior to alloSCT and who received post-transplant cyclophosphamide as part of their conditioning regimen. CONCLUSION: These findings reinforce the safety and feasibility of ICI prior to alloSCT in AML. These results suggest post-transplant cyclophosphamide may abrogate GVHD risk and severity in patients who receive ICI prior to alloSCT in AML.

Turon-Vinas, E., et al. (2021). "[Neurological complications in haematopoietic stem cell transplant patients]." Rev Neurol **73**(5): 174-183.

INTRODUCTION: Neurological complications are some of the most important complications that can occur in a patient undergoing haematopoietic stem cell transplantation (HSCT), not only because of the high mortality rate, but also because of the sequelae that appear in survivors. The causes of such complications are manifold and very often coexist in the same patient: toxicity of the conditioning regimen, graft-versus-host disease and its treatment, infections and their treatment, platelets and coagulation disorders, liver failure or arterial hypertension with low platelet count. AIMS: The aim of the present study is to provide a clinical description and to describe the risk factors for complications involving the central nervous system that may occur during the course of HSCT, in order to assist in the early detection of these disorders that may have a negative influence on the morbidity and mortality of these patients. DEVELOPMENT: The following types of neurological complications are described: central nervous system infections, vascular complications, pharmacological toxicity, metabolic complications, immune-mediated disorders and post-HSCT carcinogenesis, and effects of graft-versus-host disease and thrombotic microangiopathy on the nervous system. CONCLUSIONS: The patient undergoing HSCT is at particular risk for the development of neurological complications. Early diagnosis and treatment are needed to try to reduce the high morbidity and mortality in these patients.

Valentini, C. G., et al. (2021). "ABO Mismatch in Allogeneic Hematopoietic Stem Cell Transplant: Effect on Short- and Long-term Outcomes." Transplant Direct **7**(8): e724.

Background: The impact of ABO incompatibility (ABO-I) on hematopoietic stem cell transplant outcomes is still debated. Methods: We retrospectively investigated 432 consecutive transplants performed at our center (2012-2020). All patients but 6 were affected by hematologic malignancies. The effect of different ABO match combinations on engraftment rate, transfusion support, acute and chronic graft-versus-host disease incidences, nonrelapse mortality (NRM), disease-free survival, and overall survival was assessed in univariate and multivariate analysis. Significance was set at $P < 0.05$. Results: ABO match distribution among transplants was as follows: 223 ABO-compatible, 94 major ABO-I, 82 minor ABO-I, and 33 bidirectional ABO-I. At univariate analysis, major ABO-I delayed the engraftment of neutrophils, platelets, and erythroid cells. At multivariate analysis, major ABO-I transplants displayed delayed erythroid engraftment (odds ratio [OR], 0.51; 95% confidence intervals [CIs], 0.38-0.70; $P < 0.0001$) and hindered transfusion independence for both red blood cells (OR, 0.52; 95% CI, 0.37-0.72; $P = 0.0001$) and platelets (0.60; 95% CI, 0.45-0.86; $P = 0.0048$). Moreover, major ABO-I transplants received greater amounts of blood products ($P < 0.0001$ for red blood cells and $P = 0.0447$ for platelets). In comparison with other ABO matches, major ABO-I was associated with an increased NRM (OR, 1.67; 95% CI, 1.01-2.75; $P = 0.0427$). No effects of ABO-mismatch were found on graft-versus-host disease, disease-free survival, and overall survival. Conclusions: Major ABO mismatch delays multilineage engraftment hinders transfusion independence and increases NRM. The prognostic impact of transfusion burden in hematopoietic stem cell transplantation deserves to be explored.

Veceric-Haler, Z., et al. (2021). "Case Report: Capillary Leak Syndrome With Kidney Transplant Failure Following Autologous Mesenchymal Stem Cell Therapy." Front Med (Lausanne) **8**: 708744.

Mesenchymal stem cells (MSCs) have attracted great interest in the field of kidney transplantation due to their immunomodulatory and reparative properties. In registered clinical trials, MSCs

have been used before, at the time of, or early after transplantation and have been reported to be well-tolerated with no serious safety concerns. No results are available on the use of MSCs in the late post-transplant period. Here, we present a case report of a severe systemic complication mimicking capillary leak syndrome with ultimate kidney transplant failure after autologous transplantation of MSCs used as rescue treatment of late antibody-mediated kidney allograft rejection.

Vinodhini, M., et al. (2021). "Lenalidomide as a Potent Inducer of Graft Versus Leukemia Effect in Patients with Hematologic Malignancies at High Risk of Relapse Post Allogeneic Stem Cell Transplant." Indian J Hematol Blood Transfus **37**(3): 500-502.

Wu, Y., et al. (2021). "Evaluation of diagnostic performance of metagenomic next-generation sequencing when applied in patients after allogeneic hematopoietic stem cell transplant." Bone Marrow Transplant.

Yan, N., et al. (2021). "Case Report: Successful Chimeric Antigen Receptor T Cell Therapy in Haploidentical-Allogeneic Stem Cell Transplant Patients With Post-Transplant Lymphoproliferative Disorder." Front Oncol **11**: 709370.

Background: Epstein-Barr virus-associated post-transplant lymphoproliferative disorder (EBV-PTLD) is a potentially fatal complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Rituximab has been proven to dramatically improve the prognosis of patients with EBV reactivation and PTLD. However, reports on the curative management of refractory PTLD are scarce. Case Presentation: In this report, we describe the successful management of two patients with EBV-PTLD with chimeric antigen receptor T-cell (CAR-T) therapy. Conclusion: The present results demonstrated that patients with EBV-PTLD may benefit from CAR-T therapy and that the toxicity is manageable. Further studies are needed to verify these findings.

Yegin, Z. A., et al. (2021). "Hematopoietic Cell Transplant-Composite Risk (HCT-CR): A Novel Predictor of Prognosis in Acute Leukemia Patients Undergoing Allogeneic Hematopoietic Stem Cell Transplantation." Transplant Proc **53**(6): 2013-2020.

BACKGROUND: Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a curable treatment modality for hematologic disorders. Transplant-related mortality remains high despite prominent scientific and technologic improvements. In consideration with the potential impact of patient- and disease-related factors on transplant outcome, this retrospective study was performed to investigate the predictive role of pretransplant HCT-composite risk (HCT-CR) score in allo-HCT recipients. METHODS: A total of 313 patients with acute leukemia (male/female: 192/121; median age, 36 [18-71] years) were included in this study. The study cohort was divided into 2 subgroups based on pretransplant HCT-CR categories. The HCT-CR(lo) group included low-risk patients, and the HCT-CR(int-hi) group consisted of intermediate-, high-, and very high-risk patients. RESULTS: In the whole cohort, overall survival (OS) and 5-year OS were found to be 32.2% and 45.1%, respectively. Probability of OS was significantly better in the HCT-CR(lo) group compared with the HCT-CR(int-hi) group (P < .001). Leukemia-free survival (LFS) and 3-year LFS were 59.5% and 65.1%, respectively. Probability of LFS was better in the HCT-CR(lo) group compared with the HCT-CR(int-hi) group (P = .001). Nonrelapse mortality (NRM) and 3-year NRM were estimated to be 38.1% and 27.5%, respectively. Probability of NRM was significantly higher in the HCT-CR(int-hi) group compared with the HCT-CR(lo) group (P = .012). In multivariate analysis, HCT-CR was shown to have significant prognostic impact in acute lymphoblastic leukemia patients (P = .023; hazard ratio, 2.613; 95% CI, 1.142-5.982). CONCLUSION: Pretransplant evaluation of patient- and disease-related factors is essential for the accurate prediction of posttransplant survival. Further efforts to evolve current criteria for pretransplant risk assessment would eventuate in better transplant outcomes.

Zhao, H., et al. (2021). "Increased incidence of human papillomavirus-related precancer or second malignancy among allogeneic stem cell transplantation patients: a SEER-Medicare population study: HPV-related precancer or second malignancy in allogeneic stem cell transplant patients." Transplant Cell Ther.

INTRODUCTION: Each year more than 8,000 allogeneic stem cell transplantations (allo-SCT) are performed in the United States and approximately 30% of these patients are >/=60 years old. Allo-SCT cases have increased risk to develop human papillomavirus (HPV)-related precancer or second malignancy. It is important to evaluate HPV-related precancer or second malignancy among allo-SCT cases to develop or enhance screening and preventive practice guidelines to improve patients' survival and quality of life. OBJECTIVE: We estimated the cumulative incidence of HPV-related precancer or second malignancy in both male and female Medicare beneficiaries who received allo-SCT and compared it with non-SCT controls and non-cancer controls. MATERIALS AND METHODS: This is a retrospective matched case control study. Hematologic cancer patients aged >/=18 years who received allo-SCT between 2002 and 2011 were matched 1:5 to non-SCT controls and to non-cancer controls by age, sex, race/ethnicity, and follow-up time. Proportions of HPV-related precancer or second malignancy were estimated and compared between cases and controls

using Chi-square test and logistic regression. Kaplan-Meier cumulative incidences were estimated and compared using log rank tests. RESULTS: We identified 700 allo-SCT cases (median age of 64 years and median follow-up time post-transplant of 4.3 years) matched with 3159 non-SCT controls and 3302 non-cancer controls. About 3.7% of allo-SCT cases developed HPV-related precancer or second malignancy post-transplant, compared with 1.9% in the non-SCT controls and 1.1% in the non-cancer controls. The odds ratio of developing HPV-related precancer or second malignancy of allo-SCT cases compared with non-SCT controls and non-cancer controls was 2.0 (95% confidence interval [CI]: 1.25-3.18) and 3.5 (95% CI: 2.1-5.8), respectively. Both allo-SCT cases and non-SCT controls had significantly higher proportions and odds in developing HPV-related precancer or second malignancy than non-cancer controls. The 5-year cumulative incidence in allo-SCT cases was 5% compared with 2.1% in non-SCT controls and 1.2% in non-cancer controls. The cumulative incidence of HPV-related precancer or second malignancy in the allo-SCT was statistically significantly higher than either of the two matched control groups, and non-SCT controls had a higher cumulative incidence of HPV-related precancer or second malignancy than that in non-cancer controls. DISCUSSION: Allo-SCT cases were at increased risk of developing HPV-related precancer or second malignancy compared with non-SCT controls and non-cancer controls. Routine screening of HPV-related precancer or second malignancy in allo-SCT cases is needed to prevent HPV-related precancer or second malignancy.

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