Blood Stem Cell Research Literatures

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Abstract: 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.

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Key words: stem cell; blood; 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.

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

Akgul, N. and L. Ozdemir "Caregiver burden among primary caregivers of patients undergoing peripheral blood stem cell transplantation: a cross sectional study." Eur J Oncol Nurs. 2014 Aug;18(4):372-7. doi: 10.1016/j.ejon.2014.03.013. Epub 2014 Jun 16.

PURPOSE: This study aimed to identify caregiver burden and influencing factors on the burden in primary caregivers of peripheral blood stem cell transplantation patients within 2-12 months following transplant, indicating early recovery period after discharge. METHOD: This descriptive cross sectional study was carried out at hematopoietic stem cell transplantation outpatient units of three university hospitals in Turkey. A total of 55 patient and caregiver dyads were recruited and interviewed. The data were collected using questionnaires developed by the researchers and caregiver burden was measured with the Zarit Burden Interview. RESULTS: The mean score of Zarit Burden Interview was 28.41 (SD = 13.90). Patients' symptoms including nausea and self depreciation feeling were related to greater caregiver burden. Self-depreciation was referred to feeling undervalued. The mean score of the tool was significantly higher in caregivers who have not been educated beyond primary school and also caregivers who had lower income. Caregivers who supported their patients to fulfill physical needs and who did not receive help for meeting patients' psychological needs had statistically more elevated levels of burden. Moreover, the extent of care giving activities undertaken was positively correlated with caregiver burden scores. While positive impact of the care giving process on family relations decreased caregiver burden; negative effect increased the burden. CONCLUSIONS: This study suggests that caregiver burden of primary caregivers caring for peripheral blood stem cell transplantation patients varies by education, income status, and the extent of care giving activities undertaken. Changes in family ties and relations due to care giving effected caregiver burden.

Al-Homsi, A. S., K. Cole, et al. "Short Course of Post-Transplantation Cyclophosphamide and Bortezomib for Graft-versus-Host Disease Prevention after Allogeneic Peripheral Blood Stem Cell Transplantation Is Feasible and Yields Favorable Results: A Phase I Study." Biol Blood Marrow Transplant. 2015 Jul;21(7):1315-20. doi: 10.1016/j.bbmt.2015.02.008. Epub 2015 Mar 9.

An effective graft-versus-host disease (GVHD) preventative approach that preserves the graft-versus-tumor effect after allogeneic hematopoietic stem cell transplantation (HSCT) remains elusive. Standard GVHD prophylactic regimens suppress T cells indiscriminately and are suboptimal. Conversely, post-transplantation high-dose cyclophosphamide selectively destroys proliferating alloreactive T cells, allows the expansion of regulatory T cells, and induces long-lasting clonal deletion of intrathymic antihost T cells. It has been successfully used to prevent GVHD after allogeneic HSCT. Bortezomib has antitumor activity on a variety

of hematological malignancies and exhibits a number of favorable immunomodulatory effects that include inhibition of dendritic cells. Therefore, an approach that combines post-transplantation cyclophosphamide and bortezomib seems attractive. Herein, we report the results of a phase I study examining the feasibility and safety of high-dose post-transplantation cyclophosphamide in combination with bortezomib in patients undergoing allogeneic peripheral blood HSCT from matched siblings or unrelated donors after reduced-intensity conditioning. Cyclophosphamide was given at a fixed dose (50 mg/kg on days +3 and +4). Bortezomib dose was started at .7 mg/m(2), escalated up to 1.3 mg/m(2), and was administered on days 0 and +3. Patients receiving grafts from unrelated donors also received rabbit antithymocyte globulin. The combination was well tolerated and allowed prompt engraftment in all patients. The incidences of acute GVHD grades II to IV and grades III and IV were 20% and 6.7%, respectively. With a median follow-up of 9.1 months (range, 4.3 to 26.7), treatment-related mortality was 13.5% with predicted 2-year disease-free survival and overall survival of 55.7% and 68%, respectively. The study suggests that the combination of post-transplantation cyclophosphamide and bortezomib is feasible and may offer an effective and practical GVHD prophylactic regimen. The combination, therefore, merits further examination.

Bechtel, T., A. McBride, et al. "Aprepitant for the control of delayed nausea and vomiting associated with the use of high-dose melphalan for autologous peripheral blood stem cell transplants in patients with multiple myeloma: a phase II study." Support Care Cancer. 2014 Nov;22(11):2911-6. doi: 10.1007/s00520-014-2248-6. Epub 2014 May 17.

STUDY OBJECTIVE: The aim of this study is to evaluate the efficacy of aprepitant as part of the antiemetic regimen for high-dose melphalan conditioning in multiple myeloma patients. DESIGN: This is a prospective, single-arm study. SETTING: The study was conducted at an Academic Medical Facility. SUBJECTS: Twenty-six patients receiving high-dose melphalan with autologous stem cell support were included in this study. INTERVENTION: Eligible patients were >18 years with a diagnosis of MM undergoing high-dose melphalan followed by autologous peripheral blood stem cell transplantation (PBSCT). All patients had serum aminotransferases and total bilirubin less than 2x upper limit of normal. Treatment consisted of aprepitant 125 mg orally on day 1, followed by 80 mg orally 24 and 48 h after the initial dose; ondansetron 16 mg orally day 1; dexamethasone 12 mg orally day 1, and 8 mg orally days 2-4 with breakthrough medications as needed. MEASUREMENTS AND MAIN RESULTS: Patients were evaluated for the frequency of emetic episodes, the need for breakthrough antiemetic medication, and the mean nausea score in 24-h increments beginning 24 h after chemotherapy and continuing until 120 h. Nausea score was determined using a linear analog scale (0-10). Complete response (CR) was defined as no more than one (1) emetic episode during the evaluation period. A total of 26 patients (17 male, 9 female) were enrolled in the study. Of these, 25 (96 %) were complete responders and 24 (92 %) had no documented emetic episodes during the study period. One patient (4 %) had 1 emetic episode and one patient (4 %) had 2 emetic episodes. Some degree of nausea was reported by 23/26 patients, and the mean nausea score for the entire group over the study period was 0.7 (range 0-10). CONCLUSIONS: Addition of aprepitant to standard antiemetics resulted in low rates of delayed nausea/vomiting associated with high-dose melphalan and PBSCT, and has now become standard practice in this patient population at our institution.

Billen, A., J. A. Madrigal, et al. "Female donors and donors who are lighter than their recipient are less likely to meet the CD34+ cell dose requested for peripheral blood stem cell transplantation." Transfusion. 2014 Nov;54(11):2953-60. doi: 10.1111/trf.12720. Epub 2014 May 27.

BACKGROUND: It is of clinical relevance to recognize donors who are unlikely to meet the requested stem cell dose for transplantation, as this group may benefit from an alternative mobilization regimen. This study was performed to evaluate the frequency of unrelated donor peripheral blood stem cell (PBSC) collections that meet the target yield and the impact of donor factors on this. STUDY DESIGN AND METHODS: All sequential PBSC collections facilitated by the national registry (n = 323) from January through December 2011 were analyzed. Donor factors analyzed included age, sex, weight, and presence of a central line. RESULTS: In univariate analyses, we found that reaching the target yield was significantly associated with a higher donor weight (85.6 kg vs. 75.3 kg, $p < 0.001$), male donor sex (55% vs. 19%, $p < 0.001$), a positive difference in weight between donor and recipient (4.3 kg vs. -8 kg, $p < 0.001$), and a higher volume of blood processed (13.8 L vs. 11.9 L, $p < 0.001$). After stepwise binary logistic regression, sex ($p < 0.001$) and difference between donor and recipient weight ($p < 0.005$) remained significantly associated with target yield being met after 1 day of collection. CONCLUSIONS: This study shows than women and donors who are lighter than their recipient have a decreased likelihood of meeting the transplant physician's requested dose. New

strategies to improve mobilization in such donors are needed. These findings may also impact future donor recruitment strategies.

Bishop, D. C., A. J. Johnston, et al. "Haploidentical peripheral blood stem cell infusion in combination with chemotherapy for acute myeloid leukaemia in elderly patients." Intern Med J. 2014 Oct;44(10):1038-40. doi: 10.1111/imj.12551.

Elderly patients with acute myeloid leukaemia (AML) have a poor prognosis with standard chemotherapy. Two elderly AML patients treated with infusion of family-derived partially human leukocyte antigen (HLA)-matched peripheral blood stem cells following each cycle of chemotherapy entered morphological complete remission without graft versus host disease or major toxicity. Our results support this as a non-toxic approach for inducing a graft versus leukaemia effect in patients not suitable for allogeneic transplantation. Additional resources required for donor assessment and harvest may be reduced by using banked partially HLA-matched mononuclear cells from unrelated donors.

Bleakley, M., S. Heimfeld, et al. "Engineering human peripheral blood stem cell grafts that are depleted of naive T cells and retain functional pathogen-specific memory T cells." Biol Blood Marrow Transplant. 2014 May;20(5):705-16. doi: 10.1016/j.bbmt.2014.01.032. Epub 2014 Feb 11.

Graft-versus-host disease (GVHD) is a frequent major complication of allogeneic hematopoietic cell transplantation (HCT). Approaches that selectively deplete T cells that cause GVHD from allogeneic stem cell grafts and preserve T cells specific for pathogens may improve HCT outcomes. It has been hypothesized that the majority of T cells that can cause GVHD reside within the naive T cell (TN) subset, and previous studies performed in mouse models and with human cells in vitro support this hypothesis. As a prelude to translating these findings to the clinic, we developed and evaluated a novel 2-step clinically compliant procedure for manipulating peripheral blood stem cells (PBSC) to remove TN, preserve CD34(+) hematopoietic stem cells, and provide for a fixed dose of memory T cells (TM) that includes T cells with specificity for common opportunistic pathogens encountered after HCT. Our studies demonstrate effective and reproducible performance of the immunomagnetic cell selection procedure for depleting TN. Moreover, after cell processing, the CD45RA-depleted PBSC products are enriched for CD4(+) and CD8(+) TM with a central memory phenotype and contain TM cells that are capable of proliferating and producing effector cytokines in response to opportunistic pathogens.

Bradstock, K. F., I. Bilmon, et al. "Single-Agent High-Dose Cyclophosphamide for Graft-versus-Host Disease Prophylaxis in Human Leukocyte Antigen-Matched Reduced-Intensity Peripheral Blood Stem Cell Transplantation Results in an Unacceptably High Rate of Severe Acute Graft-versus-Host Disease." Biol Blood Marrow Transplant. 2015 May;21(5):941-4. doi: 10.1016/j.bbmt.2015.01.020. Epub 2015 Jan 27.

High-dose cyclophosphamide given early after allogeneic hemopoietic cell transplantation has been shown to be effective prophylaxis against graft-versus-host disease (GVHD) in the setting of HLA-matched myeloablative bone marrow grafts, allowing avoidance of long-term immunosuppression with calcineurin inhibitors in some patients. Whether this approach is feasible using granulocyte colony-stimulating factor (G-CSF)-mobilized peripheral blood stem cell grafts is unknown. We conducted an exploratory phase 2 trial of cyclophosphamide given at 50 mg/kg i.v. on days 3 and 4 after transplantation as sole GVHD prophylaxis in recipients of G-CSF-mobilized peripheral blood stem cell grafts from HLA-matched related or unrelated donors after reduced-intensity conditioning therapy with fludarabine, carmustine, and melphalan. Five patients, ages 52 to 67 years, with high-risk hematologic malignancies were enrolled. Four of the 5 developed severe acute GVHD of grades 3 to 4, requiring treatment with methylprednisolone and cyclosporine; 3 were steroid refractory and were given salvage therapy. One of these 4 patients died of hepatic GVHD, one died of sepsis, and 2 survived. We conclude that post-transplantation cyclophosphamide is inadequate as sole GVHD prophylaxis in the context of peripheral blood reduced-intensity conditioning transplantations from HLA-matched donors. This trial is registered at ACTRN12613001154796.

Breitkreutz, I., N. Becker, et al. "Dose-intensified bendamustine followed by autologous peripheral blood stem cell support in relapsed and refractory multiple myeloma with impaired bone marrow function." Hematol Oncol. 2015 Mar 18. doi: 10.1002/hon.2199.

Therapeutic options in heavily pretreated relapsed/refractory multiple myeloma patients are often very limited because of impaired bone marrow function. Bendamustine is effective in multiple myeloma and has a favourable toxicity profile. We hypothesized that dose-intensified bendamustine (180 mg/m2 , day 1 and 2) followed by autologous blood stem cell support (ASCS) would improve bone marrow function with low post-transplant toxicity in patients with severely impaired haematopoiesis. We analyzed 28 consecutive myeloma patients, with a median of three prior lines of therapy (range 2-7), who

had relapsed from the last treatment with very limited bone marrow function and were therefore ineligible for conventional chemotherapy, novel agents or trial enrolment. Dose-intensified bendamustine with ASCS improved haematopoiesis as reflected by increased platelet counts (median 40/nl vs 94/nl, p = 0.0004) and white blood cell counts (3.0/nl vs 4.8/nl, p = 0.02) at day +100. The median time until engraftment of platelets (>50/nl) was 11 days (0-24 days) and of white cell counts (>1.0/nl) 0 days (0-24 days). At least, a minimal response was achieved in 36% of patients. The disease stabilization rate was 50% while the median progression-free survival rate was limited to 2.14 months. Most importantly, patients were once again eligible for alternative treatments including enrolment into clinical trials. We conclude that dose-intensified bendamustine followed by ASCS is safe and feasible for multiple myeloma patients with very limited bone marrow reserve. Copyright (c) 2015 John Wiley & Sons, Ltd.

Brissot, E., X. Cahu, et al. "Initial fluconazole prophylaxis may not be required in adults with acute leukemia or myelodysplastic/myeloproliferative disorders after reduced intensity conditioning peripheral blood stem cell allogeneic transplantation." Ann Hematol. 2015 Apr;94(4):663-9. doi: 10.1007/s00277-014-2259-x. Epub 2014 Nov 21.

In the myeloablative transplant setting, the early use of fluconazole prophylaxis provides a benefit in overall survival. Recent changes in transplantation practices, including the use of peripheral blood stem cells (PBSC) and/or reduced intensity conditioning (RIC) regimen may have favorably impacted the epidemiology of invasive fungal infections (IFI) after allogeneic stem cell transplantation (allo-SCT). Yet, the impact of removing fluconazole prophylaxis after RIC PBSC allotransplant is ill known. Here, a retrospective analysis was performed comparing patients who received fluconazole as antifungal prophylaxis (n = 53) or not (n = 56) after allo-SCT for acute leukemia or myelodysplastic/myeloproliferative syndrome. Sixteen IFI were documented (14 %) at a median time of 103 days after transplantation, including eight before day +100, at a similar rate, whether the patients received fluconazole prophylaxis (13 %) or not (16 %). IFI were due mainly to Aspergillus species (87 %), and only two Candida-related IFI (13 %) were documented in the non-fluconazole group before day +100. The incidences of IFI (overall, before or after day +100) as well as 3-year overall and disease-free survival, non-relapse mortality, or acute and chronic graft-versus-host disease (GVHD) were similar between both groups. In conclusion, this study suggests that fluconazole may not be required at the initial phase of RIC allo-SCT using PBSC. This result has to be confirmed prospectively while Aspergillus prophylaxis should be discussed in this particular setting.

Celmeli, F., D. Turkkahraman, et al. "A successful unrelated peripheral blood stem cell transplantation with reduced intensity-conditioning regimen in a patient with late-onset purine nucleoside phosphorylase deficiency." Pediatr Transplant. 2015 Mar;19(2):E47-50. doi: 10.1111/petr.12413. Epub 2014 Dec 17.

PNP deficiency is a rare combined immunodeficiency with autosomal recessive mode of inheritance. The immunodeficiency is progressive with normal immune functions at birth, but then, T-cell deficiency with variable B-cell functions usually presents by the age of two yr. The only curative treatment for PNP deficiency is hematopoietic stem cell transplantation. Here, we present a 13-yr-old girl with late-onset PNP deficiency. Despite many complications of infections, she was successfully transplanted with a reduced intensity-conditioning regimen from an HLA-identical unrelated donor.

Chanswangphuwana, C., P. Kupatawintu, et al. "Successful peripheral blood stem cell mobilization using pegfilgrastim in allogeneic stem cell transplantation." Int J Hematol. 2014 Mar;99(3):318-22. doi: 10.1007/s12185-014-1507-0. Epub 2014 Jan 29.

Pegfilgrastim is produced by binding a 20,000-dalton polyethylene glycol molecule to granulocyte colony-stimulating factor (G-CSF), increasing the mass of the compound, and resulting in a longer-lasting form of G-CSF. This makes it more convenient to use pegfilgrastim as a single-day injection. This study was a prospective phase II single-center trial. Fifteen normal related donors received pegfilgrastim 12 mg subcutaneously to mobilize peripheral blood stem cells (PBSC) for allogeneic stem cell transplantation. Leukapheresis was planned to start 3 days after injection. All harvests were successful. Median number of leukapheresis was 2 days (range 1-3 days). There were 7/15 donors who only required single leukapheresis. The maximum concentration of white blood cells (WBC) and circulating CD34 cells occurred 3 days after pegfilgrastim injection (WBC: median 62,200/mul; CD34: median 69.76/mul). The median yield of CD34 cells was 6.78 x 10(6)/kg recipient weight. The median CD3 cells was 1.89 x 10(8)/kg recipient weight. The main adverse events were bone pain and headache. Median neutrophil and platelet engraftments in the recipients occurred on day 12 and day 13, respectively, after transplantation. PBSC mobilization with single-day injection of pegfilgrastim in normal donor is

feasible. Further comparisons of this protocol to standard G-CSF for allogeneic stem cell mobilization should be conducted in future.

Cioch, M., D. Jawniak, et al. "Biosimilar granulocyte colony-stimulating factor is effective in reducing the duration of neutropenia after autologous peripheral blood stem cell transplantation." Transplant Proc. 2014 Oct;46(8):2882-4. doi: 10.1016/j.transproceed.2014.09.070.

BACKGROUND: Autologous peripheral blood stem cell transplantation (APBSCT) is the standard of therapy for patients with multiple myeloma and refractory Hodgkin's and non-Hodgkin's lymphomas. Granulocyte colony-stimulating factor (G-CSF) is widely used to accelerate hematopoietic recovery after transplantation and to reduce the morbidity and mortality associated with prolonged neutropenia. Biosimilar G-CSF is approved for the same indications as the originator G-CSF. This is one of the first reported uses of a biosimilar G-CSF for neutrophil recovery after APBSCT. METHODS: A total of 23 consecutive patients with hematological malignancy (multiple myeloma, Hodgkin's and non-Hodgkin's lymphomas, and acute myelogenous leukemia) were recruited at the Department of Haematooncology and Bone Marrow Transplantation at the Medical University of Lublin. Patients (12 men and 11 women; median age, 47 +/- 13 years) received biosimilar G-CSF (Zarzio, Sandoz Biopharmaceuticals) after myeloablative chemotherapy (primarily BiCnU, etoposide, cytarabine, and melphalan or melphalan 140/200 mg/m(2)) followed by PBSCT. The median number of transplanted CD34+ cells was 4.2 +/- 0.8 x 10(6)/kg body wt. G-CSF therapy was started when absolute neutrophil count (ANC) was <0.5 x 10(9)/L and was continued until ANC reached >1.5 x 10(9)/L for 3 consecutive days. Hematopoietic recovery parameters were compared with those in the control group, which consisted of 23 consecutive patients transplanted in the period before the biosimilar G-CSF group and receiving originator G-CSF (Neupogen, Amgen). RESULTS: The mean duration of treatment with biosimilar and originator G-CSF was 14.4 +/- 5.1 and 18.6 +/- 11.5 days, respectively (P = .43). The adverse event profile was comparable between the biosimilar G-CSF and originator G-CSF groups, with similar occurrence of neutropenic fever (5 versus 6 patients) and bone pain (7 patients in each group). One patient in the biosimilar group had neutropenic enterocolitis and sepsis. There was no case of death in either group. Granulocyte recovery in the study group was as follows: mean days to ANC >0.5 x 10(9)/L was 13.0 +/- 4.0 days; to ANC >1.5 x 10(9)/L, 13.6 +/- 4.5 days; and to ANC >1.5 x 10(9)/L, 14.0 +/- 4.7 days. Mean duration until platelet recovery >20 x 10(9)/L was 16.1 +/- 4.4 days. There were no statistically significant differences between the biosimilar and originator G-CSF groups in hematopoietic recovery parameters. CONCLUSIONS: Biosimilar G-CSF is safe and effective in reducing the duration of neutropenia in patients undergoing myeloablative therapy followed by APBSCT and probably in cost savings in transplantation budgets.

Crompton, K. E., N. Elwood, et al. "Feasibility of trialling cord blood stem cell treatments for cerebral palsy in Australia." J Paediatr Child Health. 2014 Jul;50(7):540-4. doi: 10.1111/jpc.12618. Epub 2014 Jun 9.

AIM: Umbilical cord blood may have therapeutic benefit in children with cerebral palsy (CP), but further studies are required. On first appearance it seems that Australia is well placed for such a trial because we have excellence in CP research backed by extensive CP registers, and both public and private cord blood banks. We aimed to examine the possibilities of conducting a trial of autologous umbilical cord blood cells (UCBCs) as a treatment for children with CP in Australia. METHODS: Data linkages between CP registers and cord blood banks were used to estimate potential participant numbers for a trial of autologous UCBCs for children with CP. RESULTS: As of early 2013, one Victorian child with CP had cord blood stored in the public bank, and between 1 and 3 children had their cord blood stored at Cell Care Australia (private cord blood bank). In New South Wales, we counted two children on the CP register who had their stored cord blood available in early 2013. We estimate that there are between 10 and 24 children with CP of any type who have autologous cord blood available across Australia. CONCLUSIONS: In nations with small populations like Australia, combined with Australia's relatively low per capita cord blood storage to date, it is not currently feasible to conduct trials of autologous UCBCs for children with CP. Other options must be explored, such as allogeneic UCBCs or prospective trials for neonates at risk of CP.

D'Rozario, J., R. Parisotto, et al. "Pre infusion, post thaw CD34+ peripheral blood stem cell enumeration as a predictor of haematopoietic engraftment in autologous haematopoietic cell transplantation." Transfus Apher Sci. 2014 Jun;50(3):443-50. doi: 10.1016/j.transci.2014.02.021. Epub 2014 Mar 12.

INTRODUCTION: By convention, peripheral blood stem cell products for autologous transplantation are evaluated for quality by CD34(+) cell dose at the time of harvesting. A CD34(+) cell dose in excess of 2.0 x 10(6)/kg of recipient body

weight is considered adequate for haematopoietic engraftment. Viable CD34(+) cell numbers are enumerated in most laboratories using the ISHAGE single platform flow cytometric method which utilizes monoclonal antibodies to CD45, CD34 and 7 amino actinomycin D (7AAD) dye exclusion. METHODS: One hundred and six consecutive autologous transplantation procedures underwent viable CD34(+) cell enumeration at the time of harvesting and post thaw prior to re-infusion. Neutrophil and platelet engraftment and markers of haematopoietic support were analyzed. RESULTS: Mean pre-cryopreservation viable CD34(+) numbers were 4.882 x 10(6)/kg. Mean post thaw viable CD34(+) numbers were 3.234 x 10(6)/kg. Mean loss of viable CD34(+) cells with processing and cryo-preservation was 1.648 x 10(6)/kg (33%). For neutrophil engraftment, there was no significant difference between high (3.0 x 10(6)/kg) and low (<1.5 x 10(6)/kg) post thaw viable CD34(+) cell counts (p=0.545). For platelet engraftment, there was however a significant difference observed between the high and low pre infusion viable CD34(+) groups (p<0.001). Additionally, significant differences were seen between the post thaw viable CD34(+) cell count and the associated length of hospital admission, days of use of G-CSF post transplantation, use of antibiotics in the post transplantation period and transfusion support in the post transplantation period. CONCLUSION: A significant loss of viable CD34(+) cells occurs during processing, cryopreservation and thawing. Low numbers of viable CD34(+) cells infused post thaw will still result in adequate neutrophil engraftment however may delay platelet engraftment. Low viable CD34(+) cell numbers have significant effects on admission duration and use of haematopoietic supportive measures with consequent effects on healthcare resources.

ElMarsafawy, H., M. Matter, et al. "Assessment of Myocardial Function in Children before and after Autologous Peripheral Blood Stem Cell Transplantation." Echocardiography. 2015 Jun 8. doi: 10.1111/echo.12988.

BACKGROUND: Increased interest is focused on the long-term adverse effects of bone marrow transplantation. Subclinical cardiac involvement appears common in adults, but only a few reports have examined pediatric patients. MATERIALS AND METHODS: A prospective case-control study of 19 children with normal cardiac function undergoing autologous hematopoietic stem cell transplantation (HSCT) was performed. Tissue Doppler imaging (TDI) and echocardiographic measurements were obtained according to the guidelines of the American Society of Echocardiography before and 3 months after HSCT. RESULTS: Lateral mitral annulus before HSCT showed significant reduced mitral systolic annular velocity (P < 0.0001), early diastolic annular velocity (P < 0.0001), late diastolic annular velocity (P = 0.02) and prolonged isovolumetric relaxation time (IRT) (P < 0.0001) compared with control. Significant reduced mitral systolic annular velocity (P < 0.0001), early diastolic annular velocity (P = 0.0005) and Em/Am ratio (P = 0.004), with higher late diastolic annular velocity (P = 0.02) and prolonged isovolumetric contraction time (ICT) (P = 0.003) and IRT (P = 0.002) after HSCT, were observed. Investigation of lateral tricuspid annulus showed nearly similar results as the lateral mitral annulus. LV and RV Tei indices were higher before HSCT compared with control and remained high after HSCT. CONCLUSION: TDI detected subtle abnormalities in systolic and diastolic functions before and after HSCT, which suggests that a conditioning regimen may affect cardiac function.

Emir, S., H. A. Demir, et al. "Use of plerixafor for peripheral blood stem cell mobilization failure in children." Transfus Apher Sci. 2014 Apr;50(2):214-8. doi: 10.1016/j.transci.2013.12.017. Epub 2014 Jan 26.

BACKGROUND: Peripheral blood stem cell mobilization is usually performed following chemotherapy plus G-CSF in children. This standard approach may not be successful in some heavily pretreated patients undergoing mobilization. Plerixafor (AMD3100) has been used in adults as a second line mobilizing agent. Our aim is to analyze our experiences with plerixafor in children. METHODS: We retrospectively evaluated three children who received plerixafor as a second line stem cell mobilizing agent in our department in the 2010-2012 period. Data including age, sex, diagnosis, previous chemotherapy, radiotherapy details, previous harvest attempts, adverse reaction, and harvest outcome were analyzed. RESULTS: We used plerixafor in combination with G-CSF and chemotherapy or with only G-CSF seven times in three patients. All three patients were treated with different multiple chemotherapy regimens prior to stem cell harvest and failed earlier mobilization with chemotherapy plus G-CSF. The diagnoses were relapsed Hodgkin lymphoma in two and recurrent Ewing's sarcoma in one patient. We used plerixafor in combination with G-CSF and chemotherapy or with only G-CSF seven times in three patients. The harvest was successful in four of seven attempts. No adverse reaction was observed in the patients. CONCLUSION: The success rate is four out of seven attempts (57%) in our group. Although the data regarding the use of plerixafor in children is scarce, our experience also supports its use in poor mobilizer children. The use of plerixafor in children

results in effective increases in peripheral stem cell counts and reduces the risk of mobilization failure.

Fatorova, I., M. Blaha, et al. "Timing of peripheral blood stem cell yield: comparison of alternative methods with the classic method for CD34+ cell determination." Biomed Res Int. 2014;2014:575368. doi: 10.1155/2014/575368. Epub 2014 Sep 8.

Hematopoietic stem cells (HSCs), still represent a certain mystery in biology, have a unique property of dividing into equal cells and repopulating the hematopoietic tissue. This potential enables their use in transplantation treatments. The quality of the HSC grafts for transplantation is evaluated by flow cytometric determination of the CD34(+) cells, which enables optimal timing of the first apheresis and the acquisition of maximal yield of the peripheral blood stem cells (PBSCs). To identify a more efficient method for evaluating CD34(+) cells, we compared the following alternative methods with the reference method: hematopoietic progenitor cells (HPC) enumeration (using the Sysmex XE-2100 analyser), detection of CD133(+) cells, and quantification of aldehyde dehydrogenase activity in the PBSCs. 266 aphereses (84 patients) were evaluated. In the preapheretic blood, the new methods produced data that were in agreement with the reference method. The ROC curves have shown that for the first-day apheresis target, the optimal predictive cut-off value was 0.032 cells/mL for the HPC method (sensitivity 73.4%, specificity 69.3%). HPC method exhibited a definite practical superiority as compared to other methods tested. HPC enumeration could serve as a supplementary method for the optimal timing of the first apheresis; it is simple, rapid, and cheap.

Garcia-Escobar, I., L. Parrilla, et al. "Clinical experience with plerixafor as a mobilization regimen for autologous peripheral blood stem cell transplantation in patients with refractory germ cell tumors." Mol Clin Oncol. 2014 Nov;2(6):923-926. Epub 2014 Jul 29.

The purpose of this study was to report our experience with administration of plerixafor for the mobilization of hematopoietic stem cells (HSCs) in patients with refractory or recurrent germ cell tumors who were candidates for salvage therapy with high-dose chemotherapy and HSC transplantation and for whom mobilization of HSCs had not been achieved by standard therapies. This retrospective and observational study selected patients who were eligible for autologous HSC transplantation (AHSCT) and received plerixafor after failure of HSC mobilization by granulocyte colony-stimulating factor (G-CSF). A total of 5 patients (4 male and 1 female), aged 19-41 years (mean age, 29.6 years) were initially selected. Four patients (80%) achieved an adequate HSC mobilization with plerixafor and subsequently received high-dose chemotherapy followed by HSC transplantation. In these patients, the number of CD34+ cells collected following plerixafor mobilization was 1.8x106-10.3x106 cells/kg, with a peak CD34+ cell count of 7.0-32.0 cells/mul. Following HSC infusion, these 4 patients achieved a neutrophil count of >0.5x103/mm3 and a platelet count of >20,000/mul between days 10 and 14. Therefore, patients with high-risk germ cell tumors eligible for AHSCT who are refractory to mobilization by G-CSF, may benefit from the use of plerixafor, possibly to the same extent as patients with lymphoma and multiple myeloma.

Gentzler, R. D., A. M. Evens, et al. "F-18 FDG-PET predicts outcomes for patients receiving total lymphoid irradiation and autologous blood stem-cell transplantation for relapsed and refractory Hodgkin lymphoma." Br J Haematol. 2014 Jun;165(6):793-800. doi: 10.1111/bjh.12824. Epub 2014 Mar 15.

Total lymphoid irradiation (TLI) followed by high-dose chemotherapy and autologous haematopoietic stem cell transplant (aHSCT) is an effective strategy for patients with relapsed/refractory classical Hodgkin lymphoma (HL). We report outcomes for patients with relapsed/refractory HL who received TLI followed by high-dose chemotherapy and aHSCT. Pre-transplant fludeoxyglucose positron emission tomography (FDG-PET) studies were scored on the 5-point Deauville scale. Of 51 patients treated with TLI and aHSCT, 59% had primary refractory disease and 63% had active disease at aHSCT. The 10-year progression-free survival (PFS) and overall survival (OS) for all patients was 56% and 54%, respectively. Patients with complete response (CR) by PET prior to aHSCT had a 5-year PFS and OS of 85% and 100% compared to 52% and 48% for those without CR (P = 0.09 and P = 0.007, respectively). TLI and aHSCT yields excellent disease control and long-term survival rates for patients with relapsed/refractory HL, including those with high-risk disease features. Achievement of CR with salvage therapy is a powerful predictor of outcome.

Giardino, S., E. Lanino, et al. "Long-term outcome of a successful cord blood stem cell transplant in mevalonate kinase deficiency." Pediatrics. 2015 Jan;135(1):e211-5. doi: 10.1542/peds.2014-2553. Epub 2014 Dec 22.

Mevalonate kinase deficiency (MKD) is a rare autosomal recessive inborn error of metabolism with an autoinflammatory phenotype that may be expressed as a spectrum of disease phenotypes, from those with prevailing autoinflammatory syndrome and

variable response to anti-inflammatory therapies, to mevalonic aciduria, which is associated with dysmorphic features, severe neurologic involvement, and the worst prognosis. We describe a boy, aged 2 years, 10 months, with severe phenotype of mevalonate kinase deficiency who underwent allogeneic hematopoietic stem cell transplantation (HSCT) from HLA-identical unrelated cord blood because his condition had failed to improve with antiinflammatory treatment as first-line therapy and an anticytokine drug as second-line therapy. The child had a sustained remission of febrile attacks and inflammation after transplant, and during a 5-year follow-up period, psychomotor and neurologic development were normal, without signs of underlying disease or late transplant-related effects. This case confirms that allogeneic HSCT is a safe and effective cure for patients affected by MKD in whom anticytokine drugs alone are insufficient for the management of autoinflammatory syndrome and for the unfavorable outcome of the disease.

Gronier, S., E. Delmont, et al. "[Efficacy of autologous peripheral blood stem cell transplantation (auto-PBSCT) on the neuropathic manifestations in POEMS syndrome]." Rev Neurol (Paris). 2014 Jan;170(1):37-45. doi: 10.1016/j.neurol.2013.10.008. Epub 2014 Jan 8.

INTRODUCTION: POEMS syndrome (polyneuropathy, organomegaly, endocrynopathy, M-protein, and skin changes) is a rare multisystem disease associated with plasma cell dyscrasia. The efficacy of autologous peripheral blood stem cell transplantation (auto-PBSCT) reported in case series has been mainly based on hematologic criteria and clinical recovery of peripheral neuropathy dysfunctions but has not been specifically evaluated. This retrospective study aimed to analyze the efficacy of auto-PBSCT on disability and electrophysiological patterns in patients with POEMS syndrome. METHODS: Five patients presenting with POEMS syndrome received auto-PBSCT. Disability was evaluated before treatment and at 6 and 12 months using the Overall Neuropathy Limitation Scale (ONLS) and MRC sumscore of 28 muscles. Nerve conduction studies were performed before and one year after treatment, on median, ulnar, fibular and tibial nerves. RESULTS: Mean age was 60.6 years (49-70). Disease duration between first symptoms and auto-PBSCT was 15.4 months (2-33). Before auto-PBSCT, mean ONLS score was 4.2 (1-10) and mean MRC sumscore 115.8/140 (74-140). At M6, mean ONLS score decreased and mean MRC sumscore increased; both were improved in all patients at M12: mean ONLS score 3 (range 0-8) at M6 and 2.2 (range 0-7) at M12; mean MRC sumscore 118/140 (77-140) at M6 and 122.4/140 (80-140) at M12. Significant recovery in electrophysiological patterns was observed in all patients on ulnar and median nerves: before-after treatment differences were observed for motor conduction velocities (34.41 vs. 45.47 m/s; P<0.001), distal CMAP amplitudes (5.04 vs. 5.96 mV; P=0.004), and sensory conduction velocities (43.20 vs. 49.20 m/s; P=0.001). Distal CMAP amplitude remained low in fibular and tibial nerves (0.41 vs. 0.17 mV). CONCLUSIONS: Clinical and electrophysiological improvement is obvious in POEMS syndrome peripheral neuropathy within one year after treatment with auto-PBSCT, undoubtedly resulting from extensive remyelinisation and axonal regeneration. Further studies are required to examine long-term outcome in patients with POEMS syndrome given auto-PBSCT.

Gutierrez-Aguirre, C. H., A. Gomez-De-Leon, et al. "Allogeneic peripheral blood stem cell transplantation using reduced-intensity conditioning in an outpatient setting in ABO-incompatible patients: are survival and graft-versus-host disease different?" Transfusion. 2014 May;54(5):1269-77. doi: 10.1111/trf.12466. Epub 2013 Oct 28.

BACKGROUND: Graft-versus-host disease (GVHD) is a major cause of morbimortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Minor ABO incompatibility has been associated with an increased risk of GVHD. We analyzed the impact of ABO matching on patient outcome after peripheral blood, reduced-intensity allo-HSCT in an outpatient setting, and its relationship with GVHD. STUDY DESIGN AND METHODS: Data of 121 patients were included. All patients received allo-HSCT from HLA-identical siblings as outpatients using a reduced-intensity conditioning regimen. Influence of ABO matching as a risk factor for the development of GVHD and survival was analyzed using logistic regression and Cox proportional hazards regression, respectively. RESULTS: Median age was 36 years (range, 1-71 years); 88 patients were ABO identical: 13 presented major mismatch and 20 minor mismatch, with an ABO incompatibility rate of 27.3%. The median follow-up period was 54 months (range, 0.3-120 months). Minor ABO incompatibility patients presented the highest rate of acute GVHD (aGVHD; 25%), in comparison with ABO-identical (20.5%) and major ABO incompatibility patients (15.4%; p = 0.79). The highest incidence of chronic GVHD (cGVHD) occurred in the context of minor ABO incompatibility (35%), in contrast to ABO-identical (30.8%) and major ABO incompatibility (15.4%). Survival was higher for patients in the minor ABO mismatch group; however, there was no significant correlation between ABO matching status and survival (p = 0.45).

CONCLUSION: Using this type of peripheral blood stem cell transplantation, minor ABO-mismatched allo-HSCT was associated with a higher incidence of aGVHD and cGVHD and with increased survival, albeit with no significance.

Hatsuse, M., S. Fuchida, et al. "Secondary MGUS following by adenovirus-induced hemorrhagic cystitis after autologous peripheral blood stem cell transplantation in a patient with multiple myeloma." Rinsho Ketsueki. 2014 Nov;55(11):2277-82.

A 61-year-old man with multiple myeloma (IgG-kappa) received autologous peripheral blood stem cell transplantation (PBSCT) after induction of VAD in July 2009, and obtained a very good partial response. In November 2009, he was admitted to our hospital because of adenovirus-induced hemorrhagic cystitis and pneumocystis jiroveci pneumonia. The pneumonia resolved with sulfamethoxazole and steroid pulse therapy, and cystitis subsided spontaneously. In December 2009, serum protein electrophoresis showed two abnormal protein bands (APB)(IgG-lambda, IgA-lambda), different from the original M-protein, and IgG thereafter increased to 2,771 mg/dl with a concomitant increase in anti-adenovirus antibody to 4,096. In October 2010, APB disappeared. To date, he has been in stable complete remission for five years since PBSCT. The emergence of APB is considered to be a surrogate marker for long-term remission. Immune reconstitution syndrome and APB after high dose chemotherapy following PBSCT are discussed herein.

Hatsuse, M., K. Taniguchi-Yoshihara, et al. "Successful treatment with pseudo-autologous blood stem cell transplantation for an adolescent-onset multiple myeloma who relapsed after allogenic bone marrow transplantation." Rinsho Ketsueki. 2015;56(4):428-31. doi: 10.11406/rinketsu.56.428.

A 14-year-old male with multiple myeloma (IgG-lambda, ISS stage 3) received myeloablative matched unrelated bone marrow transplantation, and achieved a complete response. At 16 months after the transplantation, he relapsed. The relapse was resistant to bortezomib and thalidomide. Peripheral blood showed mixed chimerism with 10% recipient cells. Peripheral blood stem cells (PBSC) were collected and pseudo-autologous PBSC transplantation (PASCT) was performed following high-dose melphalan without graft-versus-host disease prophylaxis. Hematopoietic recovery was prompt and a partial response was obtained without graft-versus-host disease exacerbation. We have presented a rare case of adolescent-onset multiple myeloma, obtaining a transient response with PASCT following post-allogeneic transplant relapse.

Henning, R. J., P. Sanberg, et al. "Human cord blood stem cell paracrine factors activate the survival protein kinase Akt and inhibit death protein kinases JNK and p38 in injured cardiomyocytes." Cytotherapy. 2014 Aug;16(8):1158-68. doi: 10.1016/j.jcyt.2014.01.415. Epub 2014 May 10.

BACKGROUND AIMS: We hypothesized that paracrine factors from human umbilical cord blood mononuclear cells (hUCBC) activate in injured cardiomyocytes the survival protein kinase Akt and limit activation of death protein kinases JNK and p38. METHODS: We treated hUCBC with H2O2 and measured growth factors and cytokines secreted by hUCBC. We then treated cardiomyocytes with H2O2 for 24 h and measured Akt, JNK and p38 activation by means of Western blots. We also measured myocyte viability and apoptosis with the use of fluorescence-activated cell-sorting cytometry. We then investigated myocytes treated for 24 h with H2O2 plus hUCBC and myocytes without hUCBC or H2O2. Four million hUCBC were placed in transwells permeable only to hUCBC paracrine factors, and the transwells were placed in flasks with H2O2 + Dulbecco's modified Eagle's medium or in flasks with myocytes plus H2O2+Dulbecco's modified Eagle's medium. RESULTS: hUCBC increased secretion during H2O2 of hepatocyte growth factor by 338%, insulin-like growth factor by 200%, interleukin-4 by 200%, vascular endothelial cell growth factor by 192%, placental growth factor by 150%, interleukin-10 by 150% and angiogenin by 121%. H2O2 increased myocyte JNK activation by 237% and p38 activation by 60%, decreased myocyte viability by 38% and increased necrosis by 34% (all $P < 0.01$). hUCBC paracrine factors increased in myocytes with H2O2 Akt activation by >/= 25%, decreased JNK and p38 activation by > 35%, increased viability by > 22% and decreased apoptosis by > 33% (all $P < 0.05$). Akt inhibitor API-1 prevented the effects of hUCBC and enhanced H2O2 decrease of myocyte viability. Addition of JNK inhibitor SP600125 or p38 inhibitor SB203580 to myocytes plus H2O2 prevented H2O2 decrease in viability and increased hUCBC beneficial effects. CONCLUSIONS: During free radical stress, hUCBC paracrine factors activate myocyte Akt, which increases myocyte viability by decreasing activation of death-promoting protein kinases JNK and p38.

Holtick, U., J. M. Chemnitz, et al. "OCTET-CY: a phase II study to investigate the efficacy of post-transplant cyclophosphamide as sole graft-versus-host prophylaxis after allogeneic peripheral blood stem cell transplantation." Eur J Haematol. 2015 Feb 23. doi: 10.1111/ejh.12541.

Post-transplant cyclophosphamide is increasingly used as graft-versus-host disease (GvHD) prophylaxis in the setting of bone marrow transplantation. No data have been published on the use of single-agent GvHD prophylaxis with post-transplant cyclophosphamide in the setting of peripheral blood stem cell transplantation (PBSCT). METHODS: In a phase II trial, 11 patients with myeloma or lymphoma underwent conditioning with fludarabine and busulfan followed by T-replete PBSCT and application of 50 mg/kg/d of cyclophosphamide on day+3 and +4 without other concurrent immunosuppression (IS). RESULTS: Median time to leukocyte, neutrophil, and platelet engraftment was 18, 21, and 18 d. The incidence of grade II-IV and grade III-IV GvHD was 45% and 27%, with a non-relapse mortality (NRM) of 36% at one and 2 yr. After median follow-up of 927 d, overall and relapse-free survival was 64% and 34%. Three patients did not require any further systemic IS until day+100 and thereafter. Analysis of immune reconstitution demonstrated rapid T- and NK-cell recovery. B- and CD3+/CD161+NK/T-cell recovery was superior in patients not receiving additional IS. CONCLUSION: Post-transplant cyclophosphamide as sole IS in PBSCT is feasible and allows rapid immune recovery. Increased rates of severe acute GvHD explain the observed NRM and may advise a temporary combination partner such as mTor-inhibitors in the PBSCT setting.

Howard, A., P. Chitphakdithai, et al. "Evaluation of peripheral blood stem cell quality in products transported by traditional courier or commercial overnight shipping services." Transfusion. 2014 Jun;54(6):1501-7. doi: 10.1111/trf.12533. Epub 2014 Jan 3.

BACKGROUND: Peripheral blood stem cell (PBSC) products have traditionally been transported from the collection center to a transplant center using validated volunteer courier-based procedures. Evolving airline service strategies and security policies have complicated this model of product transport. This study was designed to evaluate the feasibility of transporting PBSC products using commercial overnight shipping services, while maintaining product quality, compared to courier-transported products. STUDY DESIGN AND METHODS: Five PBSC products were collected from healthy volunteer donors and divided to evaluate product quality when transported either by volunteer courier or by commercial overnight shipping service. Products were evaluated on the day of collection and at 24, 48, and 72 hours postcollection for total nucleated cell (TNC) count, cell viability, progenitor cell numbers, and progenitor cell lineage growth potential (colony-forming units [CFUs]) to assess product composition and quality associated with each cohort. RESULTS: No delivery delays were encountered and all products were received intact. Measurements of product composition and quality demonstrated no differences in TNC count (p=0.893), cell viability (p=0.409), CD34+ progenitor cell content (p=0.509), or CFU-granulocyte-macrophage growth potential (p=0.827). CONCLUSIONS: We found no difference in product viability, progenitor cell content, or product potency in PBSC products transported either by volunteer courier or by commercial overnight shipping.

Joichi, Y., I. Chijimatsu, et al. "Detection of Mucor velutinosus in a blood culture after autologous peripheral blood stem cell transplantation : a pediatric case report." Med Mycol J. 2014;55(2):E43-8.

Filamentous fungi were detected in the blood culture of a one-year-old boy after autologous peripheral blood stem cell transplantation. The patient was suspected to have aspergillosis and received micafungin. Fungi were isolated on potato dextrose agar medium and incubated at 37 for 2-5 days. Grayish, cottony colonies formed. A slide culture showed a spherical sporangium at the tips of the sporangiophores. The fungus could have been a zygomycete. The zygomycete was isolated from three blood cultures. The antifungal drug was changed from micafungin to liposomal amphotericin B, which resulted in an improvement in the patient's symptoms. Growth was observed at 37, but not 42 in a growth temperature test. Gene sequence analysis identified the fungus as Mucor velutinosus. To the best of our knowledge, this is the first time M. velutinosus has been detected in Japan, and this case is very rare. Zygomycetes are known to be pathogens that cause fungal infections in immunodeficient patients such as those with leukemia. They are difficult to identify by culture and are identified at autopsy in many cases. Therefore, culture examinations should be performed for immunodeficient patients with the consideration of zygomycetes.

Keino, D., K. Kondoh, et al. "High-dose chemotherapy followed by autologous peripheral blood stem cell transplantation for recurrent primary mediastinal malignant germ cell tumor: a case report." Pediatr Transplant. 2014 Mar;18(2):E52-6. doi: 10.1111/petr.12210. Epub 2013 Dec 28.

A 15-yr-old boy presented with an anterior mediastinal mass, multiple lung metastases and obstruction of the left brachiocephalic vein, the superior vena cava and the subclavian vein. Tumor biopsy by CT guidance confirmed a diagnosis of GCT. Five courses of BEP therapy were performed, and CT of the chest revealed reduction in the anterior

mediastinal mass and disappearance of the multiple lung metastases. We performed the anterior mediastinal mass extraction followed by adjuvant chemotherapy consisting of ICE and TIP. However, the AFP levels became elevated soon after. Abnormal accumulation was observed in the right upper lung by DW-MRI. After the operation, two courses of TI chemotherapy and two courses of HDCT followed by auto-PBSCT were performed. He was complicated with auditory disorder and renal dysfunction. Although HDCT followed by auto-PBSCT was effective for the relapsed primary mediastinal GCT, a treatment strategy avoiding late complications is warranted.

Khanafer, N., A. Neuraz, et al. "Acute graft-versus-host disease, invasive aspergillosis and Clostridium difficile colitis after peripheral blood stem cell transplantation: A complex network of causalities and a challenge for prevention." Anaerobe. 2015 Jun;33:98-100. doi: 10.1016/j.anaerobe.2015.02.007. Epub 2015 Mar 5.

Graft-versus-host disease (GVHD) is a known risk factor for invasive aspergillosis (IA), but remains poorly studied in relation to Clostridium difficile infection (CDI). We report a case of a 58-years-old patient who developed an IA within a protected room, CDI and GVHD after allogeneic allogeneic peripheral blood stem cell transplantation (PBSCT). Factors associated with this complex condition in patients receiving allogeneic PBSCT need to be identified.

Kobayashi, Y., Y. Hatta, et al. "Safety and efficacy of high-dose cyclophosphamide, etoposide and ranimustine regimen followed by autologous peripheral blood stem cell transplant for patients with diffuse large B-cell lymphoma." Leuk Lymphoma. 2014 Nov;55(11):2514-9. doi: 10.3109/10428194.2014.889827. Epub 2014 Mar 17.

We retrospectively evaluated the safety and efficacy of high-dose chemotherapy consisting of cyclophosphamide, etoposide and ranimustine (CEM) with autologous peripheral blood stem cell transplant (PBSCT) in 55 adult patients with relapsed or high-risk de novo diffuse large B-cell lymphoma (DLBCL) or DLBCL associated with follicular lymphoma. This included 36 patients in the upfront setting in their first complete remission. The median follow-up of 42 patients surviving at the time of the analysis was 52 months (range 1-159). Relapse or disease progression after PBSCT was a frequent cause of death, but no therapy-related mortality associated with PBSCT was observed. The 5-year overall survival and progression-free survival were 70.6% (95% confidence interval [CI], 54.0-82.1) and 57.0% (95% CI, 39.5-71.2), respectively. Chronic renal impairment, therapy-related myelodysplastic syndrome and prostate cancer were the major late complications. The CEM regimen is a tolerable, effective conditioning regimen for autologous PBSCT for DLBCL, with no therapy-related mortality observed.

Konuma, T., S. Kato, et al. "Comparable long-term outcome of unrelated cord blood transplantation with related bone marrow or peripheral blood stem cell transplantation in patients aged 45 years or older with hematologic malignancies after myeloablative conditioning." Biol Blood Marrow Transplant. 2014 Aug;20(8):1150-5. doi: 10.1016/j.bbmt.2014.04.005. Epub 2014 Apr 13.

We investigated whether bone marrow or peripheral blood stem cells from older sibling donors or cord blood from unrelated donors provided a better outcome in allogeneic hematopoietic stem cell transplantation for relatively older patients who were candidates for myeloablative conditioning. Clinical outcomes of 97 patients aged 45 years or older with hematologic malignancies who received unrelated cord blood transplantation (CBT) (n = 66) or bone marrow transplantation (BMT) or peripheral blood stem cell transplantation (PBSCT) from related donors (n = 31) were compared. The cumulative incidences of grades III to IV acute and extensive chronic graft-versus-host diseases were similar between both groups. Although transplant-related mortality was significantly lower after CBT compared with BMT/PBSCT from related donors (hazard ratio [HR], .29, P = .04), overall mortality (HR, .72, P = .47) and relapse (HR, 2.02, P = .23) were not significantly different after CBT and BMT/PBSCT from related donors. These data suggest that CBT could be as safe and effective as BMT/PBSCT from older related donors for relatively older patients when it is used as a primary unrelated stem cell source.

Kurnaz, F. and L. Kaynar "Peripheral blood stem cell mobilization failure." Transfus Apher Sci. 2015 May 27. pii: S1473-0502(15)00099-3. doi: 10.1016/j.transci.2015.05.006.

Autologous hematopoietic stem cell transplantation (HSCT) is an important and often life saving treatment for many hematological malignancies and selected solid tumors. To rescue hematopoiesis after high-dose chemotherapy in autologous HSCT depends on maintaining sufficient stem cells. Hematopoietic stem cells and progenitor cells expressing CD34 in the BM are mobilized into the circulation with granulocyte-colony stimulating factor +/- chemotherapy prior to autologous HSCT. One of the most important factors for success of autologous HSCT is hematopoietic stem cell (HSC) count. Minimum threshold for the engraftment of

hematopoietic cells is accepted as 2 x 106 CD34 + cells/kg especially for platelet engraftment. Below this level it is defined as stem cell mobilization failure. There are several factors affecting stem cell mobilization: prior chemotherapy (such as fludarabine, melphalan, lenalidomide) and radiotherapy, age, type of disease, bone marrow cellularity. We tried to summarize the reasons of peripheral stem cell mobilization failure.

Matsui, T., M. Hidaka, et al. "Successful treatment of bulky granulocytic sarcoma of the retroperitoneum with high-dose chemotherapy and autologous peripheral blood stem cell transplantation." J Clin Exp Hematop. 2013;53(3):235-9.

Granulocytic sarcoma is a rare disease that is rarely curable with conventional chemotherapy. This report describes a case of a patient with bulky granulocytic sarcoma of the retroperitoneum who was treated with high-dose chemotherapy and autologous peripheral blood stem cell transplantation without administering granulocyte colony-stimulating factor before stem cell collection. According to bone marrow assessment and imaging studies, the patient remained in complete remission at 5 years after transplantation. This case suggests that high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation is a therapeutic option for granulocytic sarcoma.

Matsuoka, D., M. Manabe, et al. "[Neutropenic enterocolitis after autologous peripheral blood stem cell transplantation in non-Hodgkin's lymphoma - a case report]." Gan To Kagaku Ryoho. 2014 Apr;41(4):513-5.

Here we report a case of a 59-year-old man who developed neutropenic enterocolitis(NE)after autologous peripheral blood stem cell transplantation for non-Hodgkin's lymphoma in his second complete remission.Four days after transplantation, the patient suffered from diarrhea, abdominal pain, fever, and paralytic ileus.Abdominal computerized tomography scan revealed bowel wall thickening consistent with NE.Owing to his poor performance status, only medical management, including antibiotics and bowel rest, was administered, and the patient died 18 days after transplantation.Although NE after autologous peripheral blood stem cell transplantation is a relatively rare complication, it is important to be aware that this condition can occur as one of the early complications in stem cell transplantation.

Mawatari, M., A. Isoda, et al. "A Japanese single-hospital observational trial with a retrospective case-control analysis of varicella zoster virus reactivation after autologous peripheral blood stem cell transplantation." Transpl Infect Dis. 2015 Jun 3. doi: 10.1111/tid.12406.

BACKGROUND: Varicella zoster virus (VZV) reactivation following hematopoietic stem cell transplantation (SCT) is common. To help reduce its incidence and to identify predictive factors for VZV reactivation after autologous SCT (auto-SCT), we conducted a retrospective analysis in patients with hematologic malignancy at our hospital. METHODS: We conducted a single-hospital observational trial with a retrospective case-control analysis of post-auto-SCT VZV reactivation in patients with malignant lymphoma (ML) and multiple myeloma (MM) between January 2001 and December 2010, in the Department of Hematology at our hospital. First, we analyzed the cumulative incidence of VZV reactivation during the post-SCT period. Second, we conducted a case-control analysis to identify the risk factors for VZV reactivation within 1 year after SCT. Univariate analyses were performed using Fisher's exact test for categorical variables. A multivariable model and logistic regression were used to assess the risk factors for VZV reactivation. RESULTS: We included 97 patients in this study. The median duration of follow-up was 1027 days. Forty-two patients experienced VZV reactivation after SCT, while 29 (69.0%) experienced reactivation within 1 year after SCT. The cumulative incidence was 30.7% at 1 year and 51.2% for the total observation period. Multivariate analysis showed that engraftment after day 10 was an independent risk factor for VZV reactivation (P = 0.03). CONCLUSIONS: Our study showed a high incidence of VZV reactivation in the first year after auto-SCT in ML and MM patients. Patients with delayed engraftment are at high risk for VZV reactivation and should be considered for prolonged VZV prophylaxis. This article is protected by copyright. All rights reserved.

McGuinn, C., M. B. Geyer, et al. "Pilot trial of risk-adapted cyclophosphamide intensity based conditioning and HLA matched sibling and unrelated cord blood stem cell transplantation in newly diagnosed pediatric and adolescent recipients with acquired severe aplastic anemia." Pediatr Blood Cancer. 2014 Jul;61(7):1289-94. doi: 10.1002/pbc.24976. Epub 2014 Feb 12.

BACKGROUND: Cyclophosphamide-based conditioning regimens and allogeneic hematopoietic stem cell transplantation (AlloHSCT) from matched related donors (MRD) has resulted in the highest survival rates in children and adolescents with acquired severe aplastic anemia (SAA). Time to transplant has consistently been associated with decreased overall survival. Reduced toxicity conditioning and AlloHSCT has been used

successfully in other pediatric non-malignant diseases. PROCEDURE: We piloted a risk-adapted AlloHSCT approach, using fludarabine and anti-thymocyte globulin based conditioning with high (200 mg/kg) and low (60 mg/kg) dose cyclophosphamide as upfront treatment in newly diagnosed pediatric patients with acquired SAA incorporating alternative donor sources, including cord blood. Average risk for non-engraftment patients with <10 transfusions received low dose cyclophosphamide (60 mg/kg); High Risk, those with >/=10 transfusions received conditioning regimen with higher intensity cyclophosphamide (200 mg/kg). RESULTS: Seventeen patients were enrolled and underwent AlloHSCT including 12 males and 5 females with mean age of 8 years (range 3-16), and median follow-up time of 39 months (range 1-135). Donor sources included MRD BM (6/6 [n = 9], 5/6 [n = 2]) and unrelated CB (5/6 [n = 4], 4/6 [n = 2]). Five year OS was 67.6% (37.9-85.4). Three secondary graft failures (17.6%) occurred in the low dose cyclophosphamide arm. CONCLUSIONS: Upfront treatment with risk-adapted cyclophosphamide conditioning AlloSCT is well tolerated for the management of newly diagnosed pediatric and adolescent patients with acquired SAA. However, the increased risk of graft rejection in the lower dose arm warrants additional research regarding the optimal intensity of cyclophosphamide-based conditioning regimen to reduce toxicity without increasing graft failure.

Michelis, F. V., H. A. Messner, et al. "Early lymphocyte recovery at 28 d post-transplant is predictive of reduced risk of relapse in patients with acute myeloid leukemia transplanted with peripheral blood stem cell grafts." Eur J Haematol. 2014 Oct;93(4):273-80. doi: 10.1111/ejh.12338. Epub 2014 Apr 29.

Allogeneic hematopoietic cell transplantation (HCT) is potentially curative for acute myeloid leukemia (AML). Impact of lymphocyte recovery on post-transplant outcomes has been suggested but reports are conflicting. We evaluated the impact of lymphocyte recovery at 28 d post-HCT in 191 AML patients using peripheral blood stem cells as graft. Patients were divided into those with absolute lymphocyte count (ALC) >/= 0.5 x 10(9) /L (n = 111, 58%; high ALC group) and those with ALC < 0.5 x 10(9) /L (n = 80, 42%; low ALC group), at day 28 post-transplant. With a median follow-up of 49 months, overall survival (OS) was significantly improved in the high ALC group (59% at 3 yr) vs. patients with low ALC (40% at 3 yr, P = 0.03). Cumulative incidence of relapse (CIR) was significantly lower in the high ALC group (16% at 3 yr) vs. low ALC group (36% at 3 yr, P = 0.001). Multivariable analysis for CIR demonstrated high ALC group as an independent factor decreasing relapse risk (P = 0.03, HR = 0.49, 95% CI = 0.26-0.92). Multivariable analysis for OS and non-relapse mortality did not demonstrate ALC >/= 0.5 x 10(9) /L at 28 d post-transplant to be predictive. We conclude that lymphocyte recovery with ALC >/= 0.5 x 10(9) /L at day 28 post-transplant is associated with less relapse in AML patients undergoing allogeneic peripheral blood HCT, but without survival benefit.

Moscardo, F., S. Romero, et al. "T cell-depleted related HLA-mismatched peripheral blood stem cell transplantation as salvage therapy for graft failure after single unit unrelated donor umbilical cord blood transplantation." Biol Blood Marrow Transplant. 2014 Jul;20(7):1060-3. doi: 10.1016/j.bbmt.2014.03.024. Epub 2014 Mar 28.

Graft failure is a severe treatment complication of unrelated donor umbilical cord blood transplantation (UCBT). Its incidence seems to be higher after UCBT than after transplantation with bone marrow or peripheral blood stem cells (PBSCs). The only curative option is to perform a second transplantation; however, both the ideal stem cell source and the conditioning regimen for this salvage transplantation remain unclear. We report a series of 11 patients who underwent haploidentical PBSC transplantation (PBSCT) as salvage therapy for graft failure after a previous UCBT. The reduced-intensity conditioning regimen consisted of fludarabine 150 mg/m(2) for 3 days and horse antithymocyte globulin 8 mg/kg for 4 days. Ex vivo CD34(+) positive selection was performed in all cases, and no post-transplantation graft-versus-host disease prophylaxis was used. Six of the 9 evaluable patients (67%) eventually engrafted, at a median time of 10 days. The cumulative incidence of engraftment at 28 days was 64% (95% confidence interval [CI], 35% to 92%). Two patients relapsed after PBSCT. The cumulative incidence of TRM was 55% at 2 years (95% CI, 25% to 84%), and the probability of overall survival at 2 years was 36%. Our findings suggest that haploidentical ex vivo T cell-depleted PBSCT is a feasible alternative for treating graft failure after UCBT.

Musto, P., V. Simeon, et al. "Predicting poor peripheral blood stem cell collection in patients with multiple myeloma receiving pre-transplant induction therapy with novel agents and mobilized with cyclophosphamide plus granulocyte-colony stimulating factor: results from a Gruppo Italiano Malattie EMatologiche dell'Adulto Multiple Myeloma Working Party study." Stem Cell Res Ther. 2015 Apr 17;6:64. doi: 10.1186/s13287-015-0033-1.

INTRODUCTION: A still not well defined proportion of patients with multiple myeloma (MM) and eligible for autologous stem cell transplantation (AuSCT) fails to mobilize CD34+ peripheral blood stem cells (PBSC) at all or to collect an adequate number for a safe procedure or sufficient for multiple transplants. These so-called "poor-mobilizers" are difficult to be predicted, due to marked difference across previous heterogeneous studies. METHODS: We aimed to develop a method based on simple clinical parameters for predicting unsuccessful (<2x10(6)/kg) or sub-optimal (<5x10(6)/kg) collections of CD34+ PBSC in newly diagnosed MM patients eligible for AuSCT, treated with novel agents and receiving an homogeneous mobilizing therapy with cyclophosphamide and granulocyte-colony stimulating factor (G-CSF). To this purpose, 1,348 patients enrolled in five consecutive Italian clinical trials were retrospectively analysed. Age, baseline low peripheral blood cell counts, use of lenalidomide, and haematological toxicity developed during induction were taken into account as possible factors associated with poor mobilization. RESULTS: Overall, 280 patients (20.8%) showed either sub-optimal (167 patients, 12.4%) or unsuccessful (113 patients, 8.4%) collections. All analysed parameters negatively influenced the procedure, but only age and haematological toxicity during induction maintained their significance at multivariate analysis. Based on ordinal logistic regression model, we constructed a risk heat-map where the four parameters were pooled and weighted according to their relevance as single or combined variables. This model was predictive for different probabilities of failure, suboptimal or optimal outcomes. CONCLUSIONS: We found that about one fifth of newly diagnosed MM fails to collect an adequate number of PBSC. Our model, based on a large group of patients treated frontline with novel agents and receiving the most popular mobilizing approach currently employed in Europe, is applicable in individual subjects and may contribute to the early identification of "poor mobilizer" phenotypes.

Peccatori, J., A. Forcina, et al. "Sirolimus-based graft-versus-host disease prophylaxis promotes the in vivo expansion of regulatory T cells and permits peripheral blood stem cell transplantation from haploidentical donors." Leukemia. 2015 Feb;29(2):396-405. doi: 10.1038/leu.2014.180. Epub 2014 Jun 4.

Hematopoietic stem cell transplantation (HSCT) from human leukocyte antigen (HLA) haploidentical family donors is a promising therapeutic option for high-risk hematologic malignancies. Here we explored in 121 patients, mostly with advanced stage diseases, a sirolimus-based, calcineurin-inhibitor-free prophylaxis of graft-versus-host disease (GvHD) to allow the infusion of unmanipulated peripheral blood stem cell (PBSC) grafts from partially HLA-matched family donors (TrRaMM study, Eudract 2007-5477-54). Conditioning regimen was based on treosulfan and fludarabine, and GvHD prophylaxis on antithymocyte globulin Fresenius (ATG-F), rituximab and oral administration of sirolimus and mycophenolate. Neutrophil and platelet engraftment occurred in median at 17 and 19 days after HSCT, respectively, and full donor chimerism was documented in patients' bone marrow since the first post-transplant evaluation. T-cell immune reconstitution was rapid, and high frequencies of circulating functional T-regulatory cells (Treg) were documented during sirolimus prophylaxis. Incidence of acute GvHD grade II-IV was 35%, and occurrence and severity correlated negatively with Treg frequency. Chronic GvHD incidence was 47%. At 3 years after HSCT, transpant-related mortality was 31%, relapse incidence 48% and overall survival 25%. In conclusion, GvHD prophylaxis with sirolimus-mycophenolate-ATG-F-rituximab promotes a rapid immune reconstitution skewed toward Tregs, allowing the infusion of unmanipulated haploidentical PBSC grafts.

Peerschke, E. I., C. Moung, et al. "Evaluation of new automated hematopoietic progenitor cell analysis in the clinical management of peripheral blood stem cell collections." Transfusion. 2015 Mar 21. doi: 10.1111/trf.13078.

BACKGROUND: Successful peripheral blood stem cell transplantation (PBSCT) depends on the collection and infusion of adequate numbers of peripheral blood progenitor cells (PBPCs). Several predictors of PBPC yield are used currently, including white blood cell (WBC) count and CD34 analysis. This study evaluated the utility of the new automated hematopoietic progenitor cell count available on Sysmex XN hematology analyzers (XN-HPCs) in PBSCT. STUDY DESIGN AND METHODS: The performance characteristics of XN-HPC, CD34+, and WBC analysis were compared using 107 matched peripheral blood and apheresis samples. RESULTS: Good correlation was observed between XN-HPC and CD34+ cell counts in peripheral blood (r = 0.88; slope, 0.81) and apheresis collections (r = 0.91; slope, 0.89). Moreover, peripheral blood XN-HPC and CD34 analysis showed comparable ability to predict successful PBPC harvests (>/=2 x 106 CD34+ cells/kg). At a cutoff of 20 x 106 progenitor cells/L, peripheral blood XN- HPC and CD34 analysis both showed negative predictive values (NPVs) of 100% and positive predictive values (PPVs) of 55.4 and 63%, respectively. Using an optimized cutoff of 38 x 106 progenitor cells/L, derived from receiver operating

characteristic analysis, the PPV for XN-HPC and CD34 analysis increased to 71.4 and 78.9%, respectively, with relatively unchanged NPVs (XN-HPC 97.7%, CD34+ 98.0%). In contrast, the correlation between peripheral blood WBC and CD34 analysis was poor (r = 0.48; slope, 669.85), and the peripheral blood WBC count (cutoff, 10 x 109 /L) was a poor predictor of PBPC harvest (NPV 60%, PPV 43.1%). CONCLUSION: XN-HPC compares favorably with CD34 analysis and may be a surrogate for CD34 analysis to predict optimal timing of PBPC collections.

Pineault, N. and A. Abu-Khader Advances in umbilical cord blood stem cell expansion and clinical translation, Exp Hematol. 2015 Jul;43(7):498-513. doi: 10.1016/j.exphem.2015.04.011. Epub 2015 May 10.

Umbilical cord blood (CB) is a rich source of hematopoietic stem cells (HSCs) with important applications in allogeneic stem cell transplantation. However, the low numbers of hematopoietic stem and progenitor cells (HSPCs) in banked units remain a major limitation. Protocols developed for HSPC expansion ex vivo or to improve HSPC homing to the marrow represent solutions to overcome this shortcoming. In recent decades, wide arrays of functionally divergent approaches were developed for the amplification of HSPCs. These include optimization of cytokine cocktails, coculture systems, small molecules, and delivery systems for HSPC-expansion genes. Herein, we review past and current strategies, focusing on studies that characterize the contribution of expanded CB HSPC to short- and long-term engraftment in transplantation models or in clinical trials. Also discussed are homing effectors used to promote engraftment. In summary, these studies underscore that early-acting cytokines alone can expand HSPC with short-term engraftment activity, but that robust expansion of HSPCs with long-term engraftment necessitates the synergistic action of multiple HSC-expansion agonists. In support of this, early clinical trials based on cytokine-driven HSPC-expansion protocols delivered disappointing results, whereas recent trials based on the synergistic action of cytokines and HSPC-expansion agonists reported significant improvements in engraftment and therapeutic outcomes. Conversely, molecules that enhance homing of HSPC may represent a complementary approach to improve and perhaps accelerate engraftment. Optimization of the next generation of HSPC-expansion and priming strategies should support a paradigm shift in CB transplantation in which smaller, better matched units may preferentially be used.

Pratesi, C., S. Zanussi, et al. "gamma-Herpesvirus load as surrogate marker of early death in HIV-1 lymphoma patients submitted to high dose chemotherapy and autologous peripheral blood stem cell transplantation." PLoS One. 2015 Feb 10;10(2):e0116887. doi: 10.1371/journal.pone.0116887. eCollection 2015.

Autologous stem cell transplantation (ASCT) is a feasible procedure for human immunodeficiency virus-1 (HIV-1) lymphoma patients, whose underlying disease and intrinsic HIV-1- and ASCT-associated immunodeficiency might increase the risk for gamma-herpesvirus load persistence and/or reactivation. We evaluated this hypothesis by investigating the levels of Epstein-Barr virus (EBV)- and Kaposi sarcoma-associated herpesvirus (KSHV)-DNA levels in the peripheral blood of 22 HIV-1-associated lymphoma patients during ASCT, highlighting their relationship with gamma-herpesvirus lymphoma status, immunological parameters, and clinical events. EBV-DNA was detected in the pre-treatment plasma and peripheral blood mononuclear cells (PBMCs) of 12 (median 12,135 copies/mL) and 18 patients (median 417 copies/10(6) PBMCs), respectively; the values in the two compartments were correlated (r = 0.77, p = 0.0001). Only EBV-positive lymphomas showed detectable levels of plasma EBV-DNA. After debulking chemotherapy, plasma EBV-DNA was associated with lymphoma chemosensitivity (p = 0.03) and a significant higher mortality risk by multivariate Cox analysis adjusted for EBV-lymphoma status (HR, 10.46, 95% CI, 1.11-98.32, p = 0.04). After infusion, EBV-DNA was detectable in five EBV-positive lymphoma patients who died within six months. KSHV-DNA load was positive in only one patient, who died from primary effusion lymphoma. Fluctuations in levels of KSHV-DNA reflected the patient's therapy and evolution of his underlying lymphoma. Other gamma-herpesvirus-associated malignancies, such as multicentric Castleman disease and Kaposi sarcoma, or end-organ complications after salvage treatment were not found. Overall, these findings suggest a prognostic and predictive value of EBV-DNA and KSHV-DNA, the monitoring of which could be a simple, complementary tool for the management of gamma-herpesvirus-positive lymphomas in HIV-1 patients submitted to ASCT.

Remenyi, P., L. Gopcsa, et al. "Peripheral blood stem cell mobilization and engraftment after autologous stem cell transplantation with biosimilar rhG-CSF." Adv Ther. 2014 Apr;31(4):451-60. doi: 10.1007/s12325-014-0114-z. Epub 2014 Apr 1.

INTRODUCTION: Biosimilar versions of filgrastim [recombinant human granulocyte colony-stimulating factor (rhG-CSF)] are now widely available. To date, biosimilar rhG-CSF has

demonstrated a comparable quality, safety and efficacy profile to the originator product (filgrastim [Neupogen((R))], Amgen Inc., CA, USA) in the prevention and management of neutropenia. Biosimilar rhG-CSFs have also been used to induce peripheral blood stem cell (PBSC) mobilization in patients undergoing autologous stem cell transplantation (AHSCT). The authors have examined the effectiveness of a biosimilar rhG-CSF (Zarzio((R)), Sandoz Biopharmaceuticals, Holzkirchen, Germany) in two retrospective studies across two medical centers in Hungary. METHODS: In Study 1, 70 patients with hematological malignancies scheduled to undergo AHSCT received chemotherapy followed by biosimilar rhG-CSF (2 x 5 mug) for facilitating neutrophil, leukocyte, and platelet engraftment. In study 2, 40 additional patients with lymphoid malignancies and planned AHSCT received chemotherapy followed by biosimilar rhG-CSF for PBSC mobilization. The effectiveness of treatment was assessed by the average yield of cluster of differentiation (CD) 34+ cells and the number of leukaphereses required. RESULTS: In Study 1 (patients undergoing AHSCT), the median age was 56 years and most patients were male (60%). The conditioning regimens were mainly high-dose melphalan (n = 41) and carmustine (BiCNU((R)), Bristol-Myers Squibb, NJ, USA), etoposide, cytarabine and melphalan BEAM (n = 21). Median times to absolute neutrophil and leukocyte engraftment were 9 (range 8-11 days) and 10 (8-12) days, respectively. Median time to platelet engraftment was 10.5 days (7-19 days). In Study 2, the patients' median age was 54 years and the majority (57.5%) were female. The median time interval between day 1 of mobilizing chemotherapy and first leukapheresis was 12 (9-27) days. In the autologous PBSC grafts, the median number of CD34+ cells harvested was 5.2 x 10(6)/kg (2.22-57.07 x 10(6)/kg).

Robin, M., A. Ruggeri, et al. "Comparison of unrelated cord blood and peripheral blood stem cell transplantation in adults with myelodysplastic syndrome after reduced-intensity conditioning regimen: a collaborative study from Eurocord (Cord blood Committee of Cellular Therapy & Immunobiology Working Party of EBMT) and Chronic Malignancies Working Party." Biol Blood Marrow Transplant. 2015 Mar;21(3):489-95. doi: 10.1016/j.bbmt.2014.11.675. Epub 2014 Dec 19.

Hematopoietic stem cell transplantation (HSCT) remains the only curative treatment in patients with higher risk myelodysplastic syndrome (MDS), but the choice of the optimal alternative stem cell source is still a subject of debate in patients lacking an HLA-matched sibling donor. Here, we report on a large series of patients with MDS (N = 631) transplanted either with mobilized peripheral stem cells (PBs) from unrelated donors (n = 502) or with umbilical cord blood transplant (UCB, n = 129) as alternative grafts after reduced-intensity conditioning. Neutrophil engraftment was higher after PB (98% versus 78%, P < .0001). Acute graft-versus-host disease (GVHD) was similar after PB (31%) and UCB (29%), and chronic GVHD incidence was higher after PB (41% versus 23%). Two-year nonrelapse mortality was lower after PB (31% versus 42% P = .03). There was a better overall survival (OS) and disease-free survival (DFS) after PB (49% +/- 2% versus 30% +/- 4%, P < .0001 and 44% +/- 2% versus 28% +/- 4%, P < .0001). Multivariate analysis confirmed the advantage of PB for treatment-related mortality, OS, and DFS, whereas relative risk of chronic GVHD was similar. A multivariate analysis comparing PB from a 10/10 HLA-matched donor, PB from a 9/10 HLA-matched donor, and UCB showed an advantage on treatment-related mortality, DFS, and OS only in 10/10 PB. We conclude that in MDS patients lacking an HLA-matched sibling donor, PB from a 10/10 HLA-matched unrelated donor is the preferred source of hematopoietic stem cells. HLA-mismatched unrelated donor or cord blood seem to give similar inferior results except for neutrophil engraftment, which is delayed after UCB.

Sanchorawala, V. "High dose melphalan and autologous peripheral blood stem cell transplantation in AL amyloidosis." Hematol Oncol Clin North Am. 2014 Dec;28(6):1131-44. doi: 10.1016/j.hoc.2014.08.013. Epub 2014 Sep 30.

AL amyloidosis is the most common form of systemic amyloidosis and is associated with an underlying plasma cell dyscrasia. It is often difficult to recognize because of its many manifestations. Recent diagnostic and prognostic advances include the serum-free light chain assay, cardiac MRI, and serologic cardiac biomarkers. Treatment strategies that have evolved during the past decade are prolonging survival and preserving organ function. This article outlines the role of high-dose melphalan and stem cell transplantation. This year marks the 20th anniversary for the first patient who underwent successful stem cell transplantation for this disease at Boston Medical Center.

Sekiguchi, Y., A. Shimada, et al. "A Case of Advanced Primary Thyroid Double-Hit B Cell Lymphoma in Which Complete Remission has been Maintained After High-Dose Chemotherapy and Autologous Peripheral Blood Stem Cell Transplantation Performed During the Second Remission, with a Review of the Literature." Indian J

Hematol Blood Transfus. 2014 Sep;30(Suppl 1):166-73. doi: 10.1007/s12288-013-0312-x. Epub 2014 Jan 22.

A 50-year-old woman who presented with a mass in the thyroid gland was diagnosed as having diffuse large B-cell lymphoma (DLBCL) by biopsy in August 2011. The tumor had a complex chromosomal karyotype, including 8q24 (C-MYC) and 18q21(BCL-2), and fluorescence in situ hybridization confirmed split signals of C-MYC and BCL-2. BCL-2/IgH and C-MYC/IgH fusion signals were also observed. Three courses of rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone (R-CHOP) therapy were given, followed by thyroid gland irradiation. She was achieved complete remission (CR). In January 2012, a mass appeared in the right breast, which was diagnosed as relapse by biopsy. CR was achieved again after the 4th course of R-CHOP therapy, and one course of rituximab, etoposide, methylprednisolone, cytarabine, cisplatin (R-ESHAP) therapy was given. Thereafter, CR has been maintained after high-dose chemotherapy and autologous peripheral blood stem cell transplantation. There have been only 3 reported cases of primary thyroid C-MYC and BCL-2 double-hit lymphoma, including the present case; 2 of the cases were cases of DLBCL. R-CHOP therapy, irradiation and autologous peripheral blood stem cell transplantation are expected to be effective for such patients.

Servais, S., C. Menten-Dedoyart, et al. "Impact of Pre-Transplant Anti-T Cell Globulin (ATG) on Immune Recovery after Myeloablative Allogeneic Peripheral Blood Stem Cell Transplantation." PLoS One. 2015 Jun 22;10(6):e0130026. doi: 10.1371/journal.pone.0130026. eCollection 2015.

BACKGROUND: Pre-transplant infusion of rabbit anti-T cell globulin (ATG) is increasingly used as prevention of graft-versus-host disease (GVHD) after allogeneic peripheral blood stem cell transplantation (PBSCT). However, the precise impact of pre-transplant ATG on immune recovery after PBSCT is still poorly documented. METHODS: In the current study, we compared immune recovery after myeloablative PBSCT in 65 patients who either received (n = 37) or did not (n = 28) pre-transplant ATG-Fresenius (ATG-F). Detailed phenotypes of circulating T, B, natural killer (NK) and invariant NKT (iNKT) cells were analyzed by multicolor flow cytometry at serial time-points from day 40 to day 365 after transplantation. Thymic function was also assessed by sjTREC quantification. Serious infectious events were collected up to 2 years post-transplantation. RESULTS: Pre-transplant ATG-F had a prolonged (for at least up to 1-year) and selective negative impact on the T-cell pool, while it did not impair the recovery of B, NK nor iNKT cells. Among T cells, ATG-F selectively compromised the recovery of naive CD4+, central memory CD4+ and naive CD8+ cells, while it spared effector memory T and regulatory T cells. Levels of sjTRECs were similar in both cohorts at 1-year after PBSCT, suggesting that ATG-F unlikely impaired thymopoiesis at long-term after PBSCT. Finally, the incidence and rate of serious infections were similar in both groups, while ATG-F patients had a lower incidence of grade II-IV acute graft-versus-host disease.

Singh, A. K. and M. P. Kashyap "An Overview on Human Umbilical Cord Blood Stem Cell-Based Alternative In Vitro Models for Developmental Neurotoxicity Assessment." Mol Neurobiol. 2015 Jun 4.

The developing brain is found highly vulnerable towards the exposure of different environmental chemicals/drugs, even at concentrations, those are generally considered safe in mature brain. The brain development is a very complex phenomenon which involves several processes running in parallel such as cell proliferation, migration, differentiation, maturation and synaptogenesis. If any step of these cellular processes hampered due to exposure of any xenobiotic/drug, there is almost no chance of recovery which could finally result in a life-long disability. Therefore, the developmental neurotoxicity (DNT) assessment of newly discovered drugs/molecules is a very serious concern among the neurologists. Animal-based DNT models have their own limitations such as ethical concerns and lower sensitivity with less predictive values in humans. Furthermore, non-availability of human foetal brain tissues/cells makes job more difficult to understand about mechanisms involve in DNT in human beings. Although, the use of cell culture have been proven as a powerful tool for DNT assessment, but many in vitro models are currently utilizing genetically unstable cell lines. The interpretation of data generated using such terminally differentiated cells is hard to extrapolate with in vivo situations. However, human umbilical cord blood stem cells (hUCBSCs) have been proposed as an excellent tool for alternative DNT testing because neuronal development from undifferentiated state could exactly mimic the original pattern of neuronal development in foetus when hUCBSCs differentiated into neuronal cells. Additionally, less ethical concern, easy availability and high plasticity make them an attractive source for establishing in vitro model of DNT assessment. In this review, we are focusing towards recent advancements on hUCBSCs-based in vitro model to understand DNTs.

Solomon, S. R., M. Sanacore, et al. "Calcineurin inhibitor--free graft-versus-host disease prophylaxis with post-transplantation cyclophosphamide and brief-course sirolimus following reduced-intensity peripheral blood stem cell transplantation." Biol Blood Marrow Transplant. 2014 Nov;20(11):1828-34. doi: 10.1016/j.bbmt.2014.07.020. Epub 2014 Jul 23.

Calcineurin inhibitors (CNIs) form the foundation of current graft-versus-host disease (GVHD) prophylaxis regimens. We hypothesized that a CNI-free regimen consisting of post-transplantation cyclophosphamide (PTCy) and brief-course sirolimus would reduce chronic GVHD and nonrelapse mortality (NRM) after reduced-intensity conditioning allogeneic peripheral blood stem cell transplantation (PBSCT). Twenty-six patients (median age, 61 years) underwent unmanipulated PBSCT from an 8/8 locus-matched donor (matched related donor, n = 17; natched unrelated donor, n = 9). GVHD prophylaxis consisted of PTCy and brief-course sirolimus. Donor engraftment occurred in all patients. The cumulative incidence (CI) of grade II-IV acute GVHD, grade III-IV acute GVHD, and chronic GVHD was 46%, 15%, and 31% respectively. One-year NRM was 4%. The median time to immunosuppression discontinuation was day +138. With a median follow-up of 20 months, the estimated 2-year overall survival was 71%, estimated disease-free survival was 64%, and estimated relapse incidence was 32%. In patients with a lymphoid malignancy (eg, chronic lymphoblastic leukemia, non-Hodgkin lymphoma, Hodgkin disease), 2-year disease-free survival was 100%, and there were no relapses. Good immune reconstitution was evidenced by low cytomegalovirus reactivation rate of 21% (4 of 19 at-risk patients). GVHD prophylaxis with PTCy and sirolimus achieves consistent donor engraftment, low rates of chronic GVHD and NRM, and excellent outcomes in recipients of HLA-identical related and unrelated donor allogeneic PBSCT.

Spohn, G., E. Wiercinska, et al. "Automated CD34+ cell isolation of peripheral blood stem cell apheresis product." Cytotherapy. 2015 May 14. pii: S1465-3249(15)00858-0. doi: 10.1016/j.jcyt.2015.04.005.

BACKGROUND AIMS: Immunomagnetic enrichment of CD34+ hematopoietic "stem" cells (HSCs) using paramagnetic nanobead coupled CD34 antibody and immunomagnetic extraction with the CliniMACS plus system is the standard approach to generating T-cell-depleted stem cell grafts. Their clinical beneficence in selected indications is established. Even though CD34+ selected grafts are typically given in the context of a severely immunosuppressive conditioning with anti-thymocyte globulin or similar, the degree of T-cell depletion appears to affect clinical outcomes and thus in addition to CD34 cell recovery, the degree of T-cell depletion critically describes process quality. An automatic immunomagnetic cell processing system, CliniMACS Prodigy, including a protocol for fully automatic CD34+ cell selection from apheresis products, was recently developed. We performed a formal process validation to support submission of the protocol for CE release, a prerequisite for clinical use of Prodigy CD34+ products. METHODS: Granulocyte-colony stimulating factor-mobilized healthy-donor apheresis products were subjected to CD34+ cell selection using Prodigy with clinical reagents and consumables and advanced beta versions of the CD34 selection software. Target and non-target cells were enumerated using sensitive flow cytometry platforms. RESULTS: Nine successful clinical-scale CD34+ cell selections were performed. Beyond setup, no operator intervention was required. Prodigy recovered 74 +/- 13% of target cells with a viability of 99.9 +/- 0.05%. Per 5 x 10E6 CD34+ cells, which we consider a per-kilogram dose of HSCs, products contained 17 +/- 3 x 10E3 T cells and 78 +/- 22 x 10E3 B cells. CONCLUSIONS: The process for CD34 selection with Prodigy is robust and labor-saving but not time-saving. Compared with clinical CD34+ selected products concurrently generated with the predecessor technology, product properties, importantly including CD34+ cell recovery and T-cell contents, were not significantly different. The automatic system is suitable for routine clinical application.

Strobel, J., I. Moellmer, et al. "T-cell subsets in autologous and allogeneic peripheral blood stem cell concentrates." Vox Sang. 2015 Jun 3. doi: 10.1111/vox.12289.

BACKGROUND AND OBJECTIVES: Regulatory T cells (Tregs) and other T-cell subsets are of importance in the setting of autologous and allogeneic stem cell transplantations. We conducted a study to assess the content of peripheral blood stem cell concentrates and related apheresis parameters in the autologous and allogeneic setting. MATERIAL AND METHODS: We characterized 53 donors, patients and peripheral blood stem cell concentrates (PBSC) regarding the content of CD45+ cells, lymphocytes, CD3+ cells, CD3+ CD4+ T cells, CD3+ CD4+ CD25+ T cells, CD3+ CD4+ CD25+ CD127low/negative Tregs and CD34+ cells and calculated cell yields, recruitment factors and collection efficiency for all cell types. We compared allogeneic data with autologous data. RESULTS: Autologous PBSC show significantly lower concentrations of T-cell subsets compared to allogeneic PBSC (17 112/mul CD4+ , 14 858/mul CD4+ CD25+ and 1579/mul CD3+ CD4+ CD25+ CD127low/negative Tregs in autologous compared to

65 539/mul CD4+ , 44 208+ /mul CD4+ CD25+ and 5040/mul CD3+ CD4+ CD25+ CD127low/negative Tregs in allogeneic PBSC, respectively), in contrast to CD34+ concentrations (5342/mul CD34+ in autologous compared to 2367/mul CD34+ in allogeneic PBSC, respectively).

Sugita, J., N. Kawashima, et al. "HLA-Haploidentical Peripheral Blood Stem Cell Transplantation with Posttransplant Cyclophosphamide following Busulfan-containing Reduced-Intensity Conditioning." Biol Blood Marrow Transplant. 2015 Jun 17. pii: S1083-8791(15)00410-3. doi: 10.1016/j.bbmt.2015.06.008.

Allogeneic hematopoietic stem cell transplantation (allo-SCT) using posttransplant cyclophosphamide (PTCy) has been increasingly performed. We conducted a multicenter phase II study to evaluate the safety and efficacy of PTCy-based HLA-haploidentical peripheral blood stem cell transplantation (PTCy-haploPBSCT) following busulfan (BU)-containing reduced-intensity conditioning. Thirty-one patients were enrolled; 61% patients were not in remission and 42% patients had a history of prior allo-SCT. Neutrophil engraftment was achieved in 87% patients with a median of 19 days. The cumulative incidence of grades II-IV, III-IV acute graft-versus-host disease (GVHD), and chronic GVHD at 1 year were 23%, 3%, 15%, respectively. No patients developed severe chronic GVHD. Day 100 non-relapse mortality (NRM) were 19.4%. Overall survival (OS), relapse, disease free survival were 45%, 45%, 34%, respectively, at 1 year. Subgroup analysis showed that patients who had a history of piror allo-SCT had lower engraftment, higher NRM, and lower OS than those not receiving a prior allo-SCT. Our results suggest that PTCy-haploPBSCT after BU containing reduced-intensity conditioning achieved low incidence of acute and chronic GVHD and NRM, and stable donor engraftment and low NRM particularly in patients without a history of prior allo-SCT.

Terabe, S., S. Nishiwaki, et al. "Cervical epidural hematoma in a healthy donor presenting stroke mimic symptoms: a rare adverse event following peripheral blood stem cell apheresis." Jpn J Clin Oncol. 2015 Jun;45(6):584-7. doi: 10.1093/jjco/hyv034. Epub 2015 Mar 10.

Peripheral blood stem cell apheresis from a healthy donor is indispensable for allogeneic peripheral blood stem cell transplantation. Here, we report a rare adverse event following peripheral blood stem cell apheresis. A female sibling donor, aged 61 years with an unremarkable medical history, complained of pain in the left neck and shoulder and numbness in the left upper limb 1 h after the end of peripheral blood stem cell apheresis. Paralysis of the left upper and lower limbs appeared consecutively. Computed tomography and magnetic resonance imaging of the head showed no abnormalities. Anticoagulant therapy was initiated according to the standard treatment of atherothrombotic brain infarction. Magnetic resonance imaging of the cervical cord on the following day revealed a cervical epidural hematoma. An emergency C4-C5 laminectomy was performed, and the paralysis was improved immediately after surgery. This report is the first case of cervical epidural hematoma in a healthy donor who underwent peripheral blood stem cell apheresis and presented symptoms confusingly similar to those of brain infarction.

Tipu, H. N. "Bone marrow and peripheral blood stem cell transplant: a bioinformatics approach for mismatched donor recipient pairs." J Coll Physicians Surg Pak. 2014 Sep;24(9):685-7. doi: 09.2014/JCPSP.685687.

Bone marrow and peripheral blood stem cell transplants when performed outside the family require high resolution matching of donor and recipient for human leukocyte antigen loci. Marrow registries like National Marrow Development Program in developed countries maintain record of donors and provide most suitable donor when a recipient needs a transplant. Being outside families and due to lack of shared haplotypes, these are not fully matched. Depending upon condition of patient and time available, several times one or two loci mismatched marrow has to be transplanted. This matching can be further enhanced by introduction of a recently introduced branch of science known as Bioinformatics. Combining the knowledge of computer softwares and transplant biology, it is possible to place any protein (in this case specific human leukocyte antigen alleles of potential donors and recipient) against any other, for exact amino-acids match/mismatch in user defined region and thus choosing the better-matched donor. In this write-up, an introduction of few programs available that can be used for the said purpose is given with a brief discussion of approach already used by other scientists.

Tsai, Y. Y., S. U. Chen, et al. "Live birth after single embryo transfer of autologous cryopreserved oocytes from a patient with myelodysplastic syndrome who underwent allogenic peripheral blood stem cell transplantation." J Formos Med Assoc. 2014 Dec;113(12):966-9. doi: 10.1016/j.jfma.2014.08.010. Epub 2014 Oct 5.

We report a live birth after single embryo transfer derived from autologous cryopreserved oocytes of a patient with myelodysplastic syndrome

who had undergone allogenic peripheral blood stem cell transplantation (PBSCT). In 2006, a 24-year-old female diagnosed with myelodysplastic syndrome was referred for fertility preservation before she underwent PBSCT. After controlled ovarian stimulation, 38 oocytes were retrieved for cryopreservation using a slow-freezing protocol. She was cured by PBSCT and entered menopause. After seven years, she requested thawing of the oocytes. She was prepared for a thawing cycle using hormone replacement therapy. Twenty-two cryopreserved oocytes were thawed, and 20 (91%) oocytes survived. Thirteen mature oocytes were inseminated by intracytoplasmic sperm injection. Ten (77%) oocytes were normally fertilized and 6 (60%) oocytes developed into blastocysts. Embryo transfer to her own uterus with one blastocyst was performed. Five blastocysts were vitrified. A sonographic exam at 7 weeks of gestation revealed one gestational sac with positive cardiac motion. A normal female baby weighing 2704 g was delivered at 40 weeks of gestation. A successful pregnancy from autologous cryopreserved oocytes is encouraging for cancer patients undergoing fertility preservation. For infertile cancer patients after PBSCT, we suggest the transfer of one embryo to reduce the risk of multiple pregnancies.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

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