patients with biopsy-proven disease, 43% had lymphocytosis. 100% of patients with CMV viremia and no CMV gut disease were lymphopenic. There did not appear to be any association between CMV PCR copy number and absolute lymphocyte count (r=0.016; p=0.49). There was no apparent pattern or relationship between CMV PCR copy number and degree of cytopathic changes on intestinal biopsy.

Conclusion: We hypothesized that all patients with gut-associated CMV disease would have corresponding CMV viremia. One patient with biopsy-proven disease had negative CMV PCR, so we are evaluating for potential sources of false positivity because gut-confined CMV (CMV disease without CMV viremia) is relatively uncommon in the HSCT setting. Our data support that a lack of CMV viremia does not rule out gut-associated CMV disease and that intestinal biopsy by EGD or colonoscopy is warranted in this patient population.

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Nonmyeloablative Allogeneic Hematopoietic Stem Cell Transplant in Patients with End Stage Renal Disease Requiring Dialysis – a Single Institution Experience

Mazyar Shadman [1,2], Brenda M. Sandmaier [1,2], David G. Maloney [1,2], John M. Pagel [1,2], Sangeeta Hingorani [1,3]. [1] Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA; [2] Medicine/Medical Oncology, University of Washington, Seattle, WA; [3] Pediatrics/Nephrology, University of Washington, Seattle, WA

Patients with end stage renal disease (ESRD) historically have not been offered allogeneic hematopoietic cell transplantation (HCT) because of the presumed high risk of toxicity. Use of nonmyeloablative (NMA) conditioning regimens has made allogeneic HCT a viable option for patients with variety of baseline medical comorbidities. We report our experience with NMA allogeneic HCT for patients with ESRD who were on hemodialysis (HD) or peritoneal (PD) before receiving NMA allogeneic HCT. We reviewed our institutional database at Fred Hutchinson Cancer Research Center from 1997-2013. Eight patients were on dialysis (7 on HD and 1 on PD) before they received NMA allogeneic HCT (Age: 13-67; F/M: 3/5). Six of eight patients (75%) were on dialysis when the decision for NMA allogeneic HCT was made. One patient was started on HD before the conditioning regimen and one required HD after finishing the conditioning and before the infusion of stem cells. Etiologies of ESRD included: Myeloma kidney (3), polycystic kidney disease (2), hemolytic uremic syndrome secondary to E-coli infection (1), acute tubular necrosis (ATN) (1) and acute obstructive kidney injury (AKI) (1). Four patients (50%) had previously received an autologous transplant (as part of an auto/allo tandem approach). Primary diagnosis included multiple myeloma (n=4), NHL (n=2) MDS/MPN (n=1), Wiskott–Aldrich syndrome (n=1). The conditioning regimen included Fludarabine/2GyTBI (n=3), 2GyTBI (n=1), Fludarabine/Melphalan/2GyTBI (n=1) and Fludarabine/Cyclophosphamide/2GyTBI (n=1). Fludarabine and Melphalan were administered after dialysis but with no dose reduction. Immunosuppression included Mycophenolate mofetil with cyclosporine (n=5) or Tacrolimus (n=3). Seven of eight patients died during the follow-up period (median 10.1; range 0.2-84.6 months). Two patients died within 2 weeks after transplant and neither was on dialysis at the time of referral for HCT. One had progressive Mantle cell lymphoma and was started on HD 7 days before the HCT because of obstructive AKI secondary to abdominal lymphadenopathy and the second patient had a diagnosis of multiple myeloma and required HD because of ATN after the conditioning regimen before stem cell infusion. This patient died from multi-system organ failure secondary to conditioning regimen-related toxicities (Flu/Mel/TBI). All other 7 patients survived for a median of 11.5 months (range 3.8 – 84.6). Causes of death included: CMV pneumonia, fungal CNS infection, uncontrolled bleeding during open heart surgery, relapse, and sepsis. One patient is still alive 3.8 months post auto/allo HCT. In conclusion, review of these cases indicates that NMA allogeneic SCT for patients with ESRD on dialysis at the time of referral did not lead to adverse outcomes but initiation of dialysis shortly before HCT was associated with early mortality after transplant.

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Treosulfan-Based Conditioning before Hematopoietic Stem Cell Transplantation: Analysis of Differences Between Children and Adults

Jan Styczynski. Department of Pediatric Hematology and Oncology, Collegium Medicum, Nicolaus Copernicus University, Bydgoszcz, Poland and Lidia Gil, Department of Hematology, University of Medical Sciences, Poznan, Poland

Objective: The published literature was reviewed to assess the impact of treosulfan for conditioning before allogeneic or autologous SCT to identify possible differences between children and adults with respect to toxicity, acute or chronic graft versus host disease (a/cGVHD), treatment related mortality (TRM), overall survival (OS), disease free survival (DFS).

Material and Methods: Pediatric (patients aged <18 years) data originated from EBMT megafile report (EBMT Annual Meeting 2012) and 1 study of 28 patients from India. Adult data originated from 34 studies from European countries (Germany, Poland, Italy, France, Finland, Italy), Israel (4 studies, 119 patients) and USA (1 study, 60 patients). The analysis was performed based on data published before October, 1st, 2013. Pediatric data included 604 (521 allo + 83 auto) evaluable patients out of total 871 patients reported.

Table
Results of treosulfan use in conditioning in children *vs* adults

	Children	Adults
Toxicity	Diarrhea (24%), stomatitis (22%), SGOT (25%)	Gastro-intestinal II (up to 33%), III-IV (10-29%)
aGVHD III-IV	10%	Median 23% (range 14-50)
Limited cGVHD	13%	Median 42% (range 16-72)
Extended cGVHD	6%	14-16%
3y OS	ALL-51%, AML-46%, inherited disorders-80%, hemoglobinopathies-93%	Median 61% (range 36-85)
Other	3y EFS ALL-39% AML-40%	Median 2y DFS 55% (range 35-82), RI 25% (range 15-36), 100d TRM 11.8%.

Data on adults included 644 (598 allo + 46 auto) evaluable patients out of total 835 patients reported. In pediatric cohort 165 patients suffered from malignancies, 356 patients were transplanted for non-malignant diseases; 437 underwent a first SCT, 87 had a subsequent transplant. In adult group 626 were treated for hematological malignancies and 18 for non-malignant diseases (SAA or thalassemia). No data on auto-SCT in adults were published after 2004. The majority of pediatric patients received treosulfan in dose 39-45 mg/m2 (332 patients, 62%). Most of adult patients treated after 2007 received dose of 42 mg/m2.

Results: The main indications for treosulfan use in pediatric population were non-malignant diseases (68%) or second SCT, while among adults older age (>50 years) and/or comorbidities disqualifying from myeloablative conditioning. No correlation between the given treosulfan dose and the grade III/IV toxicity was observed both in children and in adults. No association between dose and GVHD, OS, DFS, relapse incidence and TRM was found both in children and in adults.

Conclusions: Treosulfan-based conditioning with its low toxicity profile and dose-dependent myelotoxicity is a good option in children treated with non-malignant diseases. Additionally, both children and adults not eligible for conventional transplant regimen can be offered this treatment with acceptable results. Toxicity and survival were similar in children and adults, while acute and chronic GVHD incidence were higher in adult population.

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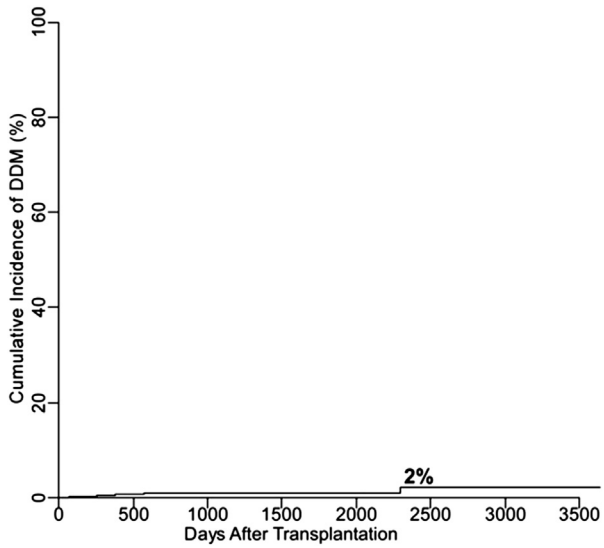
Rarity of Donor-Derived Malignancy after Allogeneic BMT with High-Dose Post-Transplantation Cyclophosphamide

Heather Jill Symons [1], Huzefa Mogri [2], Jennifer A. Kanakry [3], Richard Ambinder [4], Leo Luznik [5], Ephraim J. Fuchs [6], Richard J. Jones [7], Yvette L. Kasamon [8]. [1] Sidney Kimmel Cancer Center, Johns Hopkins University, Baltimore, MD; [2] Johns Hopkins Medical Institution, Baltimore, MD; [3] Oncology, Sidney Kimmel Cancer Center, Johns hopkins University, Baltimore, MD; [4] Sidney Kimmel Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD; [5] Hematologic Malignancies/Oncology, Johns Hopkins University School of Medicine, Baltimore, MD; [6] Oncology, Johns Hopkins University School of Medicine, Baltimore, MD; [7] Department of Oncology, The Johns Hopkins University, Baltimore, MD; [8] Oncology, Sidney Kimmel Cancer Center, Johns Hopkins University, Baltimore, MD

Donor-derived malignancy (DDM) is a rare but often fatal complication of alloBMT, with a reported incidence of 0.1-5%. AlloBMT utilizing high-dose post-transplantation cyclophosphamide (PT/Cy) as GVHD prophylaxis produces excellent rates of engraftment and low rates of acute and chronic GVHD. Because exposing the allograft to cytotoxic chemotherapy may theoretically increase the risk of DDM, we evaluated the incidence of DDM after alloBMT with PT/Cy. From 2000-2012, 790 patients (median age 51y, range 1-74y) received T-cell replete alloBMT with high-dose PT/Cy at Johns Hopkins, including 313 (40%) who received PT/Cy as sole GVHD prophylaxis. Of these transplants, 349 (44%) were HLA-haploidentical and 346 (44%) were myeloablative. Median donor age was 41y (range 13-79y). With a median follow-up of 3y (range, 0.8-9.4y) in patients without events, the 3 year PFS and OS probabilities were 42% and 56% respectively. Five cases (5/790=0.6%) of DDM were identified



as well as one case of clonal, donor-derived LGL leukemia that resolved without any therapy. By competing-risk analysis, the probability of DDM was 0.6% at 1 y, 0.8% at 5 y, and 2% overall (Figure). In the 5 identified cases of DDM, the median patient age was 41y (range 18-65 y) at BMT and median donor age was 41y (31-67y). These patients were initially transplanted for ALL (1), NHL (3), or Hodgkin lymphoma (1). Two patients received myeloablative conditioning and 3 received additional GVHD prophylaxis with mycophenolate mofetil and tacrolimus. The median time from BMT to the diagnosis of DDM was 1.3y (range 0.5-6.3y). DDMs consisted of MDS (1), AML (3), and CMML (1). All of the patients received treatment for their DDM; 2 are long term survivors and 3 died of their DDM. The incidence of developing a DDM after high-dose PT/Cy is rare, and is within the range reported for other transplant platforms.

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Ex −Vivo T Cell Depleted Allogeneic (TCD) Hematopoietic Stem Cell Transplantation for Advanced Chronic Myelofibrosis: MSKCC Experience

Roni Tamari, Ann A. Jakubowski, Esperanza Papadopoulos, Craig Sauter, Sergio A. Giralt, Hugo Castro-Malaspina. Department of Medicine, Adult Bone Marrow Transplant Service, Memorial Sloan-Kettering Cancer Center, New York, NY

Introduction: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only potentially curative treatment option for MF. The role of ex −vivo TCD allo-HSCT hasn't been reported in patients with advanced MF.

Patients: Between 5/1990-4/2013, 12 pts underwent TCD transplant at MSKCC for MF; 9 had primary MF, 2 post ET and 1 post MDS. Median age was 56 (42.7-65.5). Disease status prior to transplant per DIPSS was: intermediate-1 (4), intermediate-2 (6), and high-risk (2). Splenectomy prior to transplant was performed in 8 patients. JAK2 V617F mutation status was known on five patients and was detected on 3. Five pts received a TCD marrow graft and were conditioned with a TBI-based regimen and 7 pts received TCD peripheral blood graft and were conditioned with a chemotherapy