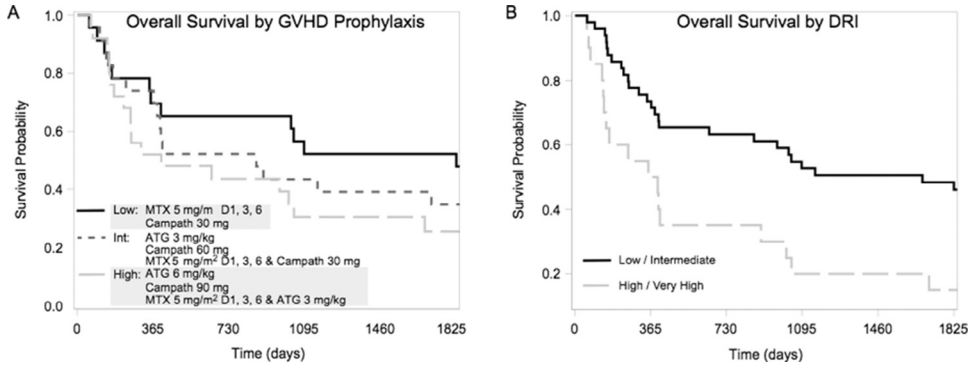


Figure 1. Kaplan Meier Survival Curves. GVHD prophylaxis regimens were divided into 3 groups (low, intermediate, high) based upon expected intensity of immunsuppression. The respective regimens are shown (Figure 1A inset). By multivariable analysis, there was a statistically significant difference in overall survival (OS) according to GVHD prophylaxis group ($P = .0337$). OS was also associated with Disease Risk Index (DRI), dichotomized to account for low numbers of "Low" and "Very High" risk subjects (Figure 1B, $P = .0018$).

Results: 71 patients were enrolled. The median age was 58 (range 28-69) with 58% men and 42% women. 37 patients received HLA-matched related donor (MRD) stem cell grafts, and 34 patients received either matched unrelated donor (MUD) or HLA-mismatched grafts. The median HCT-Comorbidity Index (CI) score was 3 (range 0-8, HCT-CI score: 0 = 12 pts, 1-2 = 22 pts, ≥3 = 36 pts). 56% of the patients were intermediate risk by Disease Risk Index (DRI) score with the remaining being very high (1%), High (29%), low (12%) and undetermined (2%). Estimated median survival time based on DRI for low/int was 1674 days (CI 646-2920) versus 375.5 days (CI 136-1018) ($P = .003$) for DRI high/very high pts. A total of 9 (13%) patients developed grade 3-4 acute GVHD, with 5 of the 20 long-term survivors having extensive chronic GVHD. The degree of immunosuppression for the 8 GVHD prophylaxis regimens was classified as low, moderate and high based upon the use of MTX and the dose intensity of ATG or Campath. By multivariable analysis, including donor type, HCT-CI and DRI**,** an association between worse overall survival (OS) and increased degrees of immunosuppression was observed ($P = .0337$, Figure 1). The worse OS rate was attributable to both increased relapse related mortality (RRM) and non-relapse mortality (NRM), primarily due to infection.

Conclusion: Continuous infusion, reduced dose, busulfan and fludarabine can be safely administered to patients who are ineligible for myeloablative conditioning either because of age or comorbidities. Highly T cell depleting GVHD prophylaxis regimens are associated with worse OS due to increases in both NRM and RRM.

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Allogeneic Stem-Cell Transplantation for Chronic Lymphocytic Leukemia

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Introduction: Chronic Lymphocytic Leukemia (CLL) is the most common form of adult leukemia. Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is the only known therapy with curative potential in poor risk disease.EBMT recommends Allo-HSCT for CLL in following situations:non-response or early relapse (within 12 months) after purine analogues, relapse within 24 months after having achieved a response with purine-analogue-based combination therapy or autologous transplantation and patients with p53 abnormalities.

Method: We retrospectively evaluated 7 CLL (5 M/2 F) patients who underwent Allo-HSCT rescue from 2007 up to now at Ankara University Department of Hematology.

Results: Patient characteristics are shown in Table 1. The median age of the group was 47 (range, 40-56).The median time from diagnosis to Allo-HSCT was 46 months (range, 7-82).2 of 7 (29%) patients were chemo-refractory, 5 of 7 patients (71%) were in complete remission prior to Allo-HSCT.Except 1 patient, all patients received reduced intensity conditioning regimen.6/7 (86%) patients were transplanted from related HLA full-matched donor whereas 1 patient re-

Table 1
Patient Characteristics

Pt no	Age/Sex	Disease Status at Transplantation	Conditioning Regimen	HLA Match/Stem Cell Source	CD34 Count (x10^6/kg)	Engraftment (day)	AGVHD/ CGVHD	Ex/ Relaps	os
1	41/M	CR	FLU+TBI	Full match related/PB	7,1	17	–/–	+/–	48
2	40/F	Refractory	CY+TBI	Full match related/PB	4,07	22	–/+	–/+	116
3	53/M	CR	FLU+BU+CY+ATG	1 mismatch unrelated/PB	6,98	13	+/+	+/–	57
4	56/M	Refractory	FLU+BU+CY	Full match related/PB	2,5	16	+/–	+/–	19
5	44/F	CR	FLU+CY+TBI	Full match related/BM	3,8	6	–/–	–/+	60
6	46/M	CR	FLU+TBI	Full match related/PB	7,42	13	–/+	+/–	65
7	52/M	CR	FLU+TBI	Full match related/PB	6	28	–/–	–/+	121

ceived stem cell from HLA 1 mismatch unrelated donor.The median CD34 count during Allo-HSCT was 5,38 × 10^6/kg. Peripheral blood was the stem cell source in 6/7 (86%) the patients.For graft-versus host disease prophylaxis, patients received cyclosporine plus methotrexate. The patients achieved engraftment at a median of 16 days after HSCT (range, 6-28). Disease responses after the allo-HSCT were as follows:4/7 (57%) complete remission, 3/7 (43%) not responded.Two of seven (29%) patients had acute graft versus host disease whereas 3/7 (43%) diagnosed with chronic graft versus host disease. Four of seven (57%) died after allo-HSCT.Three of seven (43%) patients were relapsed and clinically stable after different treatment modalities (1 patient treated with high-dose metilprednisolon and rituximab, 1 patient received ibrutinib, 1 patient got rituximab and bendamustin). Median OS of the patients were 69 months (range, 19-121).

Conclusion: In high-risk patients, allo-HSCT remains the therapy with potentially long-term sustainable responses.The targeted therapies could potentially improve transplant associated outcomes.

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Outcomes of Pharmacokinetically Targeted Busulfan-Based Conditioning Regimen for Patients with Myelodysplastic Syndrome and Acute Myelogenous Leukemia Undergoing CD34 Selected Allogeneic Hematopoietic Stem Cell Transplantation

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Introduction: Conventional allogeneic hematopoietic cell transplantation (allo-HSCT) is an established therapy for the treatment of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). CD34 selected allo-HSCT has been shown to yield similar survival rates as unmodified transplant but with significantly lower incidence of acute and chronic GVHD. This type of transplant is done mostly in the context of a myeloablative conditioning (MAC) regimen and a common chemotherapy regimen is busulfan (bu), melphalan and fludarabine with ATG. The aim of this study is to evaluate PK directed bu dosing strategy in pts with MDS and AML undergoing CD34 allo-HSCT.

Patients and Methods: This was a retrospective analysis that included 166 adult pts with advanced MDS (RAEB-1 and higher) (N = 66) or AML (N = 100) who underwent CD34 selected allo-HSCT between 2000-2014. Pts who were conditioned with bu at a total daily dose of 3.2 mg/kg (given q6 or q24 over 3 days), melphalan 140 mg/m2, fludarabine 125 mg/m2 and ATG were included. Median age was 63 yrs (28-73). There were 76 women (46%). HCT-CI was >3 in 70 pts (43%). Donors were HLA matched in 129 pts or mismatched in 37 pts, all unrelated. Pharmacokinetics were assessed after the first bu dose and adjustment was made to achieve a targeted total daily busulfan AUC of 4100-5200 min*umol/L (goal 4700 min*umol/L).

Results: The median initial bu dose was 60 mg for q6h dosing (19-82) and 240 mg for q24h dosing (170-310). In 96 pts (58%) there was a need for dose adjustment after the first PK resulted; dose increase was required in 59 pts (36%). The median total bu exposure for all pts was 13213 min*umol/L (6938-17291). After first dose PK adjustments, range of total exposure with 1st quartile (Q1) was 6938-12652, 2nd quartile (Q2) 12653-13213, 3rd quartile (Q3) 13214-14113 and 4th quartile (Q4) 14114-17291. Females were more likely to have lower bu exposure (Q1), while males were more likely to have higher exposure (Q2 and Q3) and male and female distribution was similar in Q4 ($P = .025$). Univariate analysis of clinical outcomes by bu exposure quartiles showed worse NRM for pts in Q4 (14113.49-17291.81): day 100 cumulative incidence of NRM was 11.9% (95% CI: 2-21.8), and by 1 year 33.5% (95% CI: 19%-48.1%), $P = .036$. It remained significant in multivariable regression analysis after adjusting for other parameters that were found to predict for NRM including donor status, gender and HCT-CI HR of 1.86 (95% CI: .88-3.91), $P = .048$.

Conclusions: In this cohort of MDS and AML patients undergoing CD34 allo-HSCT results suggest that total bu exposure higher than 14113 min*umol/L (Q4) was associated with increased NRM. Lower bu exposure was not associated with increased relapse or decreased survival. Targeting a lower total exposure of bu between 12652-14113 umol*min/L or total daily bu AUC of 4200-4700 umol*min/L could result in a decreased risk of NRM in this patient population.

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Nivolumab is Effective in Relapsed Refractory Hodgkins Lymphoma Patient Following Mismatched Allogeneic Stem Cell Transplantation

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Nivolumab, a programmed death 1 (PD-1) blocking antibody, is approved in relapsed or refractory Hodgkin's lymphoma (HL) and exerts its effect by blocking a negative regulator of T-cell activation thus enhancing immune effector function against lymphoma. To our knowledge, Nivolumab has never been evaluated after allogeneic stem cell transplantation in HLA-mismatched setting. Here we describe a 23-year-old male with Classical Hodgkin's Lymphoma Nodular Sclerosing type who relapsed after autologous stem cell transplantation. He was treated with Brentuximab and achieved a complete response prior to undergoing allogenic stem cell transplantation. The conditioning was reduced intensity Fludarabine and Busulfan (Flu/Bu2) and graft source was bone marrow from an HLA-A antigen mismatched unrelated donor. The Graft versus Host Disease (GVHD) prophylaxis was thymoglobulin, Bortezomib, Tacrolimus, and Methotrexate. The patient had an uneventful post-transplant course with no GVHD but unfortunately around day+100 he presented with night sweats and pruritus. A CT Chest/Abdomen subsequently showed small volume lymphadenopathy (LAD) in the pretracheal, supraclavicular and para-aortic region. The biopsy of para-aortic LN confirmed relapsed disease. Immunosuppression was subsequently discontinued but a repeat positron emission tomography (PET/CT) scan showed progressive disease. He was treated with five cycles of Brentuximab, without significant benefit. The patient declined further therapy and donor lymphocyte infusion and was lost to follow up for eight months.

The patient sought treatment at a different facility and received a single cycle of Bendamustine but returned to our