(CLS) and idiopathic pulmonary syndrome (IPS). Plasma angiopoietin-2 (ANG2), VEGF, soluble thrombomodulin (sTM), D-dimer, plasmin-α2 plasmin inhibitor complex (PIC), soluble IL2 receptor (sIL2R) and C-reactive protein (CRP) were measured. Multiple characteristics including plasma markers were evaluated for their association with the incidence of TRCs and the probability of overall survival (OS) and non-relapse mortality (NRM).

**Results:** Median follow-up duration of surviving patients after transplant was 3.9 years. The source of graft was bone marrow from unrelated donor in 40%, cord blood in 29% of the patients. Eighty-four percent of the patients received myeloablative conditioning regimen.

Accumulative incidence of total non-infectious TRCs was 70.4% at day 100. ED was observed in 62 patients: SOS ($n=19$), TAM ($n=28$), CLS ($n=10$) and IPS ($n=5$). Acute GVHD occurred in 108 patients: grade I ($n=33$), grade II ($n=44$), grade III/IV ($n=31$). OC developed in 32 patients.

When cumulative incidences of ED at day 100 were compared according to biomarker levels at transplant, the incidence was significantly higher in the high ANG2 ($\geq$1.8ng/ml; $P<0.001$), high sIL2R ($\geq$0.5U/ml; $P=0.0027$), and high sTM ($\geq$2.4ng/ml; $P=0.011$). When patients were stratified by the three markers, the incidence of ED was 63.8% (high ANG2 plus either high sIL2R or high TM; $n=47$), 10.8% (all low; $n=74$), and 27.9% (others; $n=68$). No significant difference was observed in the cumulative incidence of grade 3 to 4 acute GVHD at day100 between high- and low- groups of any biomarkers tested, although weak association was observed with ANG2 in a cohort of patients who developed acute GVHD.

With adjusted analysis, the 3-year NRM rate was significantly higher in high groups of ANG2 ($\geq$1.8ng/ml; HR 2.27; $P=0.0036$) and CRP ($\geq$1.9 mg/dl; HR 2.97; $P<0.001$). When patients were divided by a combination of the two markers, NRM was 12.4% (group A; both low; $n=115$), 28.9% (group B; either high; $n=82$), and 63.2% (group C; both high; $n=26$). The 5-year OS was also significantly different among the above three groups (A, 63.7%; B, 48.0%; C, 21.0%; $P<0.001$). Multivariate analysis revealed that group B (HR, 1.80; $P=0.0093$) and group C (HR, 2.93; $P<0.001$) along with disease risk and HLA-mismatch donor were independently associated with poor OS.

**Conclusion:** Combination of multiple biomarkers at transplant had significant powers for predicting the occurrence of ED and survival. The high predictability would make them useful for real-time clinical judgment and early intervention.

**Disclosure of Interest**: None declared.

## P629

## Second allogeneic haematopoietic stem cell transplantation using reduced-intensity conditioning regimen as treatment for haematological malignancies relapsing following first allogeneic haematopoietic stem cell transplantation

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**Introduction:** Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is an effective treatment for haematological malignancies. But the management of patients relapsing after allo-HSCT is controversial. The use of a second allo-HSCT has been reported to be associated with improved disease-free survival compared with chemotherapy, cytokine therapy and donor leukocyte infusion. We performed a retrospective survey of second allo-HSCT for haematological malignancy relapse in our institution.

**Materials (or patients) and methods:** We have retrospectively analyzed the records of 333 adult patients who underwent allo-HSCT in our hospital between April 2005 and December 2014. Thirty-five patients were eligible for a second allo-HSCT, having relapsed after the first allo-HSCT.

**Results:** The underlying disease was acute myeloid leukemia (AML) in 22 patients, myelodysplastic syndrome (MDS) in 4, acute lymphoblastic leukemia (ALL) in 7, myeloproliferative disorder (MPD) in 1, and malignant lymphoma (ML) in 1. Ages ranged from 17 to 66 years (median 38); 10 patients were female and 25 were male. The median time to relapse following the first allo-HSCT was day +259 (range 42 - 2115). Twelve patients achieved a 2nd complete remission (CR), and 3 patients were in a 3rd CR at the second allo-HSCT. 20 patients were non-responders (NR) at the second allo-HSCT. All patients were treated with reduced-intensity conditioning regimens; fludarabine, melphalan and low-dose total body irradiation (TBI) containing regimens. The donor source was sibling bone marrow (BM) or peripheral blood stem cells (PBSC) in 8 patients (including HLA mismatched PBSC in 4), unrelated BM in 15, and unrelated cord blood in 12. Currently six out of 35 patients (17%) are alive and disease-free after second allo-HSCT (range 289 - 1837). All of these patients achieved a state of CR at the second allo-HSCT, had a remission lasting over 6 months following the first allo-HSCT and developed chronic graft versus host disease (GvHD). Transplant-related mortality (TRM) within day +100 occurred in 9 patients (26%). Twenty-one patients (60%) developed chronic GvHD. The median time to relapse following the second allo-HSCT was day +158 (range 69 - 525). In total, 29 patients died. The causes of death were relapse (17 patients; 59%), GvHD (3 patients), infection (6 patients) and other causes (3 patients).

**Conclusion:** Our study suggests that second allo-HSCT as treatment for relapse of haematological malignancy after first allo-HSCT is effective in selected patients who have achieved a CR state at second allo-HSCT and remission lasting for 6 months following the first allo-HSCT.

**Disclosure of Interest**: None declared.

## P630

## Late complications (LC) and quality of life (QOL) after allogeneic stem cell transplantation (allo-SCT)

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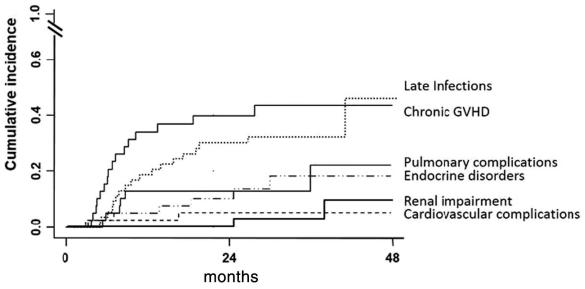
**Introduction:** While the features of early complications of allo-SCT are well known, data is still sparse in the setting of LC and especially long term QOL after allo-SCT.

**Materials (or patients) and methods:** This report analyzed the features of LC and QOL after day +100 in 39 consecutive patients who underwent allo-SCT in our institution and

**[P629]** Table. 1 Treatment and Clinical outcomes of long-term disease free survivors

| Sex | Age | Diagnosis | Diagnosis at 2nd allo-HSCT | Donor source | conditioning regimen | GvHD prophylaxis | relapse following first allo-HSCT | chronic GvHD | following second allo-HSCT |
|---|---|---|---|---|---|---|---|---|---|
| female | 54 | AML | 3rd CR | unrelated BM | Flu/Mel/TBI 2Gy | FK506 + short MTX | day +1055 | Yes | day +1837 |
| female | 17 | AML | 2nd CR | unrelated BM | HDAC/Flu/Mel/TBI 2Gy | FK506 + short MTX | day +313 | Yes | day +1769 |
| female | 27 | ALL | 2nd CR | unrelated cord blood | VP16/Flu/Mel/TBI 2Gy | FK506 + miniMTX | day +1070 | Yes | day +1734 |
| female | 23 | AML | 3rd CR | unrelated cord blood | HDAC/Flu/Mel/TBI 2Gy | FK506 + miniMTX | day +738 | Yes | day +1501 |
| male | 41 | ALL | 3rd CR | unrelated cord blood | VP16/Flu/Mel/TBI 2Gy | FK506 + miniMTX | day +1810 | Yes | day +822 |
| male | 28 | ALL | 2nd CR | HLA miss-matched sibling PBSC | VP16/Flu/Mel/TBI 2Gy | FK506 + short MTX + ATG | day +652 | Yes | day +289 |




survived for a minimum of 2 years after transplantation. QOL was assessed in a cross-sectional study by the use of EORTC QLQ-C30 and SF-36 questionnaires.

**Results:** The median age of 19 female and 20 male recipients was 44 (range, 18-58) years. In all, 12 patients (31%) had a lymphoid malignancy, while 27 patients (69%) were diagnosed with myeloid malignancies. In total, 27 patients (69%) received peripheral blood stem cells, while 12 patients (31%) received unmanipulated bone marrow. Twenty-five grafts (64%) were obtained from HLA identical siblings, 13 (33%) from HLA matched unrelated donors and 1 (3%) from a haploidentical donor. Twenty patients (51%) received a myeloablative conditioning and 19 patients received fludarabine, busulfan and ATG-based reduced-intensity conditioning regimen (49%). With a median follow-up of 945 days (range, 725-1451), chronic GVHD (cGVHD) was the most prevalent late complication with a cumulative incidence of 44% (95%CI, 27-59) at 2 years. Late infections, mostly viral, also had a cumulative incidence of 44% (95% CI 28-60). The cumulative incidence od organ-specific LC was 58% (95% CI 24-82%). Pulmonary complications were often related to cGVHD for a cumulative incidence of 22% (95%CI, 6-44). The cumulative incidence of cardiovascular complications was 5% (95%CI, 1-15) and of renal impairment 9% (95%CI, 1-28). Endocrine disorders had a cumulative incidence of 18% (95%CI, 7-34) involving thyroid dysfunction in 5% (95% CI 1-15). A secondary malignancy occured in one patient as metastatic pancreatic adenocarcinoma and led to the patient's death. In the univariate analysis, age of patients, type of conditioning, donor or source of the cells did not influence the incidence of LC. However, patients with grade II-IV acute GVHD had significantly ($P = 0.02$) higher cumulative incidence of organ-related LC (67%, 95%CI 28-88) compared to patients with grade 0-I acute GVHD (23%, 95% CI 8-43). In this series, 33 patients (85%) accepted to participate in the QOL survey. Among these, 15 patients (45%) had developed cGVHD after allo-SCT. Overall, patients had good global quality of life with a general health score of 50 (SD 18) in the SF-36 and mean global QOL group score of 62 (SD 22) in the QLQ-C30 questionnaire. Compared to the group without cGVHD, patients with cGVHD had significantly lower QOL in terms of emotional well-being and social functioning in the SF-36 questionnaire. Similarly, in the EORTC QLQ-C30, patients with cGVHD had significantly lower QOL in terms of emotional, cognitive and social functioning and reported significantly more financial disturbancies ($P < 0.05$ for all comparisons). Interestingly, there were no significant diferences in the terms of physical functioning and symptom scales between these two groups of patients.

**Conclusion:** In summary, patients who have clinically severe acute GVHD after allo-SCT have a higher probability of late organ-related complications. Among these complications, chronic GVHD remains to be a most prevalent problem that affects QOL, requiring long-term appropriate psychological support for patients.

**Disclosure of Interest**: None declared.

# Conditioning regimen II

## P631

## Sequential chemotherapy associating Thiotepa, Etoposide and Cyclophosphamide followed by reduced-intensity conditioning allogeneic hematopoietic stem cell transplantation for the treatment of refractory hematological malignancies

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**Introduction:** The results of conventional allo-SCT in refractory hematologic malignancies are poor. The sequential FLAMSA strategy has shown promising results in refractory AML. We developed a new sequential approach combining an induction chemotherapy associating Thiotepa, Etoposide and Cyclophosphamide (TEC), which has a broad anti-tumor activity, followed by RIC regimen for the treatment of wide spectrum refractory hematologic malignancies.

**Materials (or patients) and methods:** 22 patients with refractory hematologic malignancies received an allo-SCT after a TEC-RIC regimen. Patients received total dose Thiotepa 10 mg/Kg, Etoposide 400 mg/m$^2$, Cyclophosphamide 1600 mg/m$^2$ (D-15 to -10), and after a 3 days rest, Fludarabine 150 mg/m$^2$, iv Busulfan 6.4 mg/Kg (D-6 to -2) and Thymoglobuline 5 mg/Kg (D-3 and -2). Graft versus host disease (GVHD) prophylaxis consisted in Cyclosporine and Mycophenolate Mofetil. High dose Cyclophosphamide post-transplant (PT-CY) was added in case of a haplo donor. Prophylactic DLI was scheduled by D120 after withdrawal of immunosuppression.

**Results:** Median age was 44 years (range 17-65). All patients had refractory hematologic diseases: 11 AML, 6 ALL, 3 CMML and 2 DLBCL. 80% leukemic patients had persistent marrow blasts at transplant (median $= 20\%$) and 10/11 AML had poor cytogenetic. Sequential allo-SCT was performed after a median of 2 lines of prior treatment (range 1-4) including 2 auto and 3 allo-SCT. Five patients were transplanted with a sibling donor, 9 with an unrelated HLA 10/10 ($n = 7$) or 9/10 ($n = 2$) donor and 8 with a haplo-identical donor. Graft source was peripheral blood stem cells in 86%. Median follow up was 6.5 months (range, 1.5-20). All patients engrafted, median time for neutrophils and platelets recovery were 14 (range, 11-25) and 11 (range, 7-50) days, respectively. Toxicities of conditioning were all reversible and included 54% of mucositis (median grade $= 2$), 1 case of VOD, 4 other grade 1-2 liver toxicities (18%) and 5 grade 1 to 3 renal toxicities (22%). CMV and EBV reactivations occurred in 54% of patients, all of them responded to preemptive treatments, and 40% of patients developed hemorrhagic cystitis with positive BK virus, independently of the use of PT-CY. At D30, median blood chimerism was 99.5% donor (range, 96-100) and all patients reached complete morphological remission. Cumulative incidence of grade II-IV and III-IV acute GVHD at day 100 were 32% and 22%, respectively. Among 15 patients evaluable after D100, 7 developed chronic GVHD. Non relapse mortality (NRM) was 11% at D100 and 17% at 6 months. Relapse incidence was 30% at 6 months and 1 year. Eight of 13 patients evaluable after D120 without relapse (61%) received preemptive DLI at a median of 153 (range, 90-216) days, 6 of them were alive in CR at last follow up. Eight patients died, 3 of relapse, 2 of infection and 3 of GVHD. At 1 year, the probability of overall survival was 45%. There was no difference in outcomes between haplo and non haplo-SCT.

**Conclusion:** We describe a relatively safe and highly effective sequential conditioning regimen prior to allo-SCT that could be proposed to any type of refractory and high risk