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P739

Austrian Stem Cell Transplantation Registry (ASCTR)—preparing for the future

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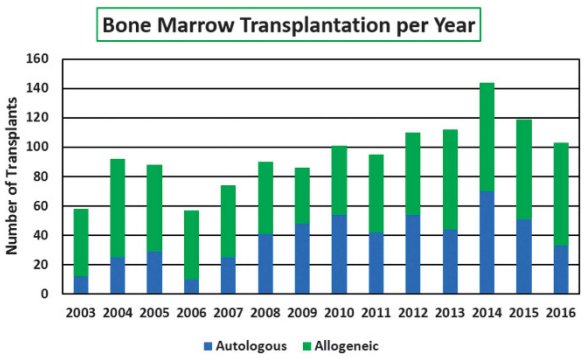
Since 2000, when Promise was introduced, the Austrian Stem Cell Transplantation Registry (ASCTR) has been using the EBMT database as national registry database. We have been collecting MED-A-Data of all HSCT performed in Austria since 1978 from all registered transplant centers, including by now 3832 allogeneic and 5897 autologous transplants. Main disease categories in the allogeneic setting are AML ($n = 1233$) and Precursor Lymphoid Neoplasms ($n = 665$), in the autologous setting NHL ($n = 1384$) and Multiple Myeloma ($n = 2190$). The ratio adult versus paediatric transplants is 8269 versus 1460. In addition, we use the EBMT data base for collecting data on family donor outcome. Furthermore, data on stem cell harvests has been collected locally since 2005. The ASCTR is obliged to report data on patient and disease demographics quarterly to the Austrian health authorities. For this purpose we keep these data in a local database that is linked to the EBMT database. Central data entry through the ASCTR includes immediate queries to reporting centers if data are missing or incorrect. Additional data quality checks are done on an annual basis when the data is analysed for the annual report on HSCT in Austria. This procedure has proved feasible and useful over the past years. So far, only two Austrian centers, both pediatric, have entered their data directly using Promise. All other Med-A data sets have been sent as paper version by the centers and have been entered centrally via the ASCTR. From 2017 onwards the Austrian centers are obliged to switch to online data entry, in accordance with the requirements of the EBMT to go paper free in 2017. We plan to do the necessary training courses for data entry within the first two to four months of the coming year, allowing a smooth transition. In order to encourage members of the Austrian Group for Stem Cell Transplantation (AGSCT) to use ASCTR data as starting point for new studies and other research projects, the ASCTR will focus on data quality issues including patient and disease demographics such as pretransplant comorbidities, disease stage, cytogenetic and molecular markers and follow-up reports to allow transplant outcome analyses that will be included in the annual report of the Ministry of Health in the near future. Each contributing center should have easy access to frequently needed analyses of their own data to be used for quality control of local transplant practices and for preparation of JACIE audits. Furthermore, donor follow-up data will be linked to a national database located at the transplant agency of the Ministry of Health to allow analyses on safety issues of hematopoietic stem cell donation and long-term side-effects. As an alternative to the use of EBMT database downloads for local analyses the establishment of a separate database combining all Austrian transplant and harvest centers has been discussed within the AGSCT. Besides being more costly, this strategy would result in decreased use of the EBMT database and centers, providing a minimum of data to EBMT since the vast majority of data collected would be stored in another database separate from EBMT. Hopefully, within due time a decision among our centers regarding database use will be made to foster further research projects and outcome analyses of both transplant recipients as well as donors.

Disclosure of conflict of interest: None.



P740

Blood and Marrow Transplantation Program experience at King Hussein Cancer Center

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The Blood and Marrow Transplantation (BMT) Program in King Hussein Cancer Center (KHCC), the first and only comprehensive program in Jordan, was established in 2003. The BMT team constitutes of specialized physicians, nurses, clinical pharmacists, Laboratory technologists, social workers, and nutritionists. Regular multidisciplinary weekly meeting are held to ensure patients' needs are met for pre and post BMT periods. We report our experience since the inception of the program. A retrospective analysis of the BMT database at KHCC of all patients received stem cell transplantation between Match 2003 and October 2016 was conducted. A total of 1318 patients: adults 714 (54%) and pediatrics 604 (46%) were transplanted at a mean of 94 transplant per year. Most of patients were Jordanians (81%).

The remaining (19%) were referred from neighboring countries. 784 (59%) allogeneic transplantation and 534 (41%) autologous. 966 (76%) were for malignant disorders and 322 (24%) were for non-malignant conditions. Most of allogeneic BMT were from matched living elated donor 694 (89%); mismatched siblings 21 (3%), haploidentical siblings 37 (5%), unrelared cord blood 29 (4%) and matched unrelated donor (MUD) 3 (0.4%). The chance of finding a fully matched related donor within Jordanian families was 65%. 544 (69%) received traditional myeloablative conditioning and 217 (28%) received reduced intensity conditioning. 23 (3%) with Severe Combined Immunodeficiency function didn't receive conditioning. The 100-day transplant related mortality (TRM) for both autologous and allogeneic transplantation is trending down, and for the last 7 years, it did not exceed 5% for autologous and 12% for allogeneic transplants. Main causes of TRM were sepsis and pulmonary infections. Table 1 depicts the number and percentage of different disease types underwent transplantation. The BMT program at KHCC is a young yet growing program. A steady growth of the program with a TRM trending down, and overall results comparable to international institutions has been observed. The program is on the verge of major expansion, a full member of EBMT and in the process of applying for JACIE-FACT accreditation.
Disclosure of conflict of interest: None.

Table 1 [P740]

Disease	*Number of transplants (%)*
Malignant	
Leukemia	372 (37%)
Lymphoma	305 (31%)
Plasma cell disorder	159 (16%)
Solid tumor	118 (12%)
Myelodysplastic/myeloproliferative disorder	42 (4%)
Non-malignant	
Hemoglobinopathy	149 (46%)
Bone marrow failure	117 (36%)
Immunodeficiency disorder	44 (14%)
Inherited disorders	12 (4%)

P741
Confounders of Consent: a Single-Centre Analysis of Predictors of Consent in a Stem Cell Transplant Service (SCT)

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Patient and outcome data collection is an integral component of participation in national and international SCT registries. Data reporting and research projects require prospective consent before collation and transmission. We performed an audit of consent for research data collection and transmission at our centre and identified factors associated with lack of consent status prior to SCT. Patients and Method: A retrospective cohort study identified 1,117 patients receiving 1,283 transplants between August 1987 and June 2016. Minimum follow-up was 100 days. 43.4% were consented and 56.6% were non-consented (i.e., deceased before consent [$n = 403$], explicitly refused consent [$n = 2$], alive and on active follow-up but did not respond [$n = 114$], and lost to follow [$n = 113$]). Factors contributing to consent status were identified and impact on survival outcomes was assessed. Results: Non-consented vs consented patients were significantly more likely to suffer post-transplant mortality (63.9% vs 27.2, $P < 0.001$), be lost to follow-up (17.9% vs 14%, $P < 0.001$), be from outside major city (29.3% vs 22%, $P < 0.001$), be < 61 y/o at first transplant (70.4% vs 60.4%, $P < 0.001$), receive autologous cells as first transplant (74.7% vs 65.8%, $P < 0.001$), to suffer more relapse (41% vs 34.6%, $P = 0.003$) and die within 100days post-transplant (14.7% vs 1.9%, $P < 0.001$). Median time to relapse is 293 days vs 364 days ($P = 0.039$). Using logistic regression analysis, 71.1% ($P < 0.001$) of variance in consent rates could be predicted by the significant variables with survival status and day 100 mortality being the most highly correlated variables predicting lack of consent. Overall survival (OS) rates ($P < 0.001$) and disease-free survival (DFS) rates ($P < 0.001$) were consistently higher for consented vs non-consented patients at all time points assessed post-SCT. (Figures 1, 2) Conclusion: High rates of non-consent in data collection and transmission may impact on the utility of national and international SCT databases. In this single-centre retrospective audit, high rates of non-consent were associated with younger age at transplant, regional residence and poorer outcome. This study highlights a selected cohort of patients who may benefit from additional strategies for obtaining consent for data collection and transmission prior to SCT.
Disclosure of conflict of interest: None.

P742
Previously Published

P743
Regular feedback of data quality measures improves the reliability of outcomes analysis

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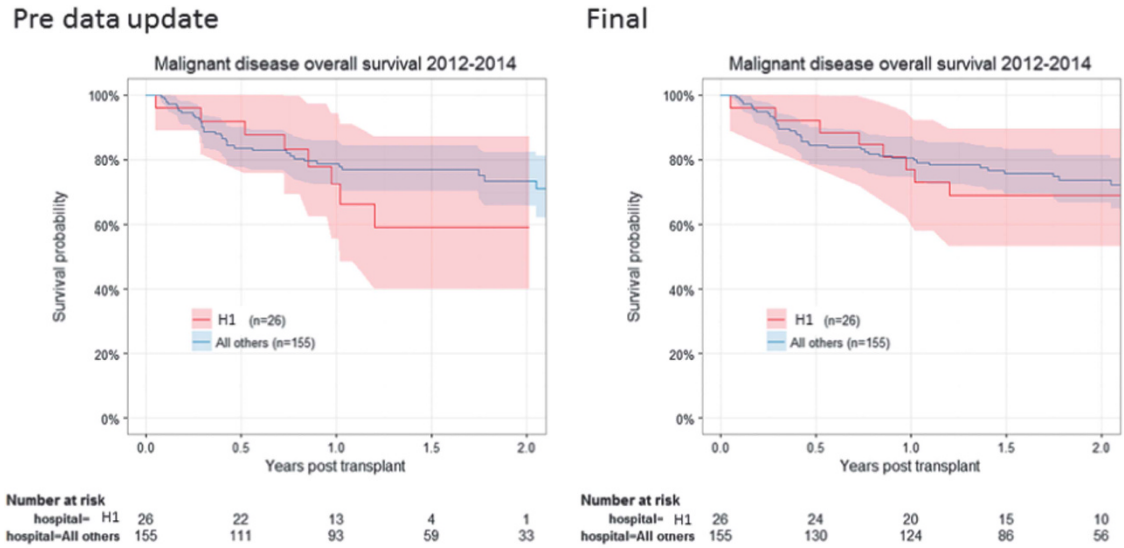
[1]Australasian Bone Marrow Transplant Recipient Registry

The Australasian Bone Marrow Transplant Recipient Registry (ABMTRR) has been collecting details of haemopoietic stem cell transplants in Australia and New Zealand since 1992. The registry is managed by the Bone Marrow Transplant Society of Australia and New Zealand, and whilst registry reporting is not mandatory, it is believed the ABMTRR has close to full enumeration of transplant activity in these two countries. However, collection of follow up data varies from centre to centre and can be an administrative burden for hospital respondents. The online database system developed in 2013 has helped to streamline the data submission process. Data quality monitoring, previously performed for the whole database, is now performed for each centre and reported back to them for comparison with the total database each quarter. Database reports are available to help address these data quality measures, as well as requirements for specific analyses. Measures of data quality that will impact most on analysis of outcomes for benchmarking purposes have been defined. These include the percentage of patients with one year follow up data available and the percentage of patients with survival data in the past two years (or death recorded), which we use as an indicator of data currency. These measures have been reported back to centres quarterly since June 2015. Database reports are also available to help prepare for analysis of nominated subgroups, such as the Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG) benchmarking analysis. From June 2015 to December 2016, the percentage of patients with one year data available increased from 91% to 95% overall, with 33 out of 50 hospitals now over 95%. In the same period, data currency improved overall from 64% to 71%, with 35 hospitals now over 70% and 17 over 80%, an improvement from 20 and 7 hospitals respectively. In preparation for paediatric benchmarking analysis, online reports simplified data updates, resulting in narrower confidence limits for the survival analysis shown below. Identifying and focusing on key reporting parameters has improved data quality allowing for more precise transplant outcomes analysis. This will enable

Figure 1 [P743]



more accurate and timely service reporting, individual hospital benchmarking and transplantation research.
Disclosure of conflict of interest: None.

P744
The Challenges in Achieving Accurate MEDA Reporting for Multiple Myeloma Autologous Recipients
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Myeloma (MM) is the most common indication for autologous BMT in adults. Obtaining accurate diagnostic/follow up data to use in MEDA submissions can be challenging, since referral data can be patchy or inaccurate. (1) All 93 first autologous transplants performed by the South Wales Blood and Marrow Transplant Programme for MM in 2014 and 2015 were reviewed. Data on transplant protocols (reflecting referral data) was compared with source data obtained for EBMT MEDA reporting. 5 parameters were assessed: diagnosis date, myeloma subtype, disease status at BMT, Durie-Salmon stage, and HCT-CI score. (2) Data was extracted from electronic/paper records from referring hospitals. The results are summarised in Table 1. Inaccuracies were seen across all 5 parameters. For the exact date of diagnosis, only 46/93 (49.4%) had an accurate date; the rest were either inaccurate or were missing/incomplete. The inaccuracies ($n = 25$, 26.9%) ranged from 1 day to 433 days; median = 15 days. For disease status at BMT (using the International Myeloma Working Group response criteria), 17/93 (18.3%) were inaccurate. The inaccuracies were instances of responses being overstated ($n = 10$) or understated ($n = 7$). Post review: 7 were upstaged: PR-VGPR = 3, VGPR-sCR = 1 and CR-sCR = 3. 10 were down staged: CR-VGPR = 7 (6 due a lack of a negative immunofixation test/ bone marrow), VGPR-PR = 1, and PR-progression = 2. Inaccuracies in HCT-CI score ($n = 7$, 9.6%) were simply down to clinicians not thoroughly checking pre-BMT tests against the HCT-CI criteria. In Durie-Salmon staging inaccuracies ($n = 14$, 15.1%), 6 were a result of staging being applied when not technically possible i.e. not all diagnostic tests were actually performed. Six were stated as stage I/II, but post review were in fact stage III. Two involved differences between the A/B component (serum creatinine) of the staging. Most inaccuracies were attributed to clinicians not having access to the primary source data at time of transplant. Although requested at referral, compliance by referrers is generally poor. Source data is obtained by the Data Manager.

Table 1

Parameters Reviewed (n = 93)
Exact Date of Diagnosis (Full date)
Accurate = 46 (49.4%)
Inaccurate = 25 (26.9%)
No date entered = 4 (4.3%)
Partial date (month and year) = 18 (19.4%)
Myeloma subtype
Accurate = 75 (80.6%)
Ig/Light chain type not documented = 18 (19.4%)
Disease status at BMT
Accurate = 74 (79.6%)
Inaccurate = 17 (18.3%)
Unclear = 2 (2.2%)
Durie-Salmon Stage
Accurate = 56 (60.2%)
Inaccurate = 14 (15.1%)
Missing = 23 (24.7%)
HCT-CI Score ($n = 73$)
Accurate = 54 (74%)
Inaccurate = 7 (9.6%)
Missing = 12 (16.4%)

Data in referral letters is often at variance with source data. This probably reflects the practice of dictating letters without reference to the patients' records. Access to source data reveals inaccuracies in up to 26% of any given parameter. Although inaccuracies in reporting the date of diagnosis may not affect overall clinical outcomes. Inaccuracies in other parameters such as myeloma subtype, disease status at BMT, Durie-Salmon stage and HCT-CI are of particular importance and may have significance in the interpretation of registry data. The data shows the importance of having access to good data management support to allow accurate MEDA reporting.
Disclosure of conflict of interest: None

P745
Adoptive immunity transfer from donor renders protective effect against hepatitis B reactivation after allogeneic transplantation for patients with resolved hepatitis B infection—A large endemic medical center report
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Taiwan is an endemic area for Hepatitis B virus (HBV) infection, with the majority of adult residents exposed to HBV during their childhood and 15-20% became HBV carrier. Reactivation of HBV, sometimes fulminant hepatic failure occurred, used to be one major issue after hematopoietic stem cell transplant (HSCT), now can be efficiently prevented by antiviral drug. However, reactivation of HBV by reverse seroconversion (HBV-RS) was sporadically reported in the patients who were so-called "cured or resolved HBV infection" (rHBV, HBsAg-negative, anti-HBc-positive) after immunotherapy, biological therapy, and after allo-HSCT. In this retrospective cohort study, we aim to report on the incidence, risk factors, and outcome of HBV-RS. **Patients and Methods**: Between January 2005 and September 2016, 914 consecutive patients receiving allo-HSCT at National Taiwan University Hospital were included. Every patient and their donors had complete HBV serology check-up, including HBsAg, anti-HBs, and anti-HBc. Of them, 448 (49%) patients were identified as rHBV. Their transplant data were collected following the EBMT Registry data collection forms and manuals. HBV-RS was defined as the detection of positive HBsAg and or detectable HBV DNA after Allo-HSCT. Donor with HBsAg positive was excluded. Liver biopsy was performed whenever clinically necessary to confirm the etiology. Univariate and multivariate analysis were performed using Cox proportional hazard regression model. This study was approved by the hospital Research Ethics Committee. Results There were 25 events (5.6%) of HBV-RS in 448 patients with rHBV after allo-HSCT. The cumulative incidence of HBV reactivation after allo-HSCT were 9% (95% CI: 0.06–0.13) at 3 years and 12.6% (95% CI: 0.08-0.18) at 5 years. The median time of HBV-RS was 1.2 years (ranges 0.02–11.3). Among them, 22 cases who had their HBV DNA PCR data examined all have concurrent HBV DNA activation (range 26 to $>1\times10^7$ copies/mL). Six patients developed HBV flare (ALT levels >5 times the upper limit), and none had fulminant hepatitis or died of hepatic failure. The risk factors for HBV-RS were: age over 50, reduced intensity conditioning, presence of chronic graft-versus host disease (cGVHD), and donors negative for anti-HBs in the univariate analyses. In multivariate analysis, cGVHD was significantly associated with higher risk of HBV RS (HR: 10.656, 95% CI: 1.4-78.9, $P=0.0205$). Interestingly, donors with anti-HBs significantly reduced the recipient risk of HBV RS (HR: 0.359, 95% CI: 0.16-0.81, $P=0.0138$), suggesting an adoptive donor immunity protection. Those patient developed episodes of HBV RS had a better 5-year OS than those without (63.6% vs 44.79%, $P=0.0118$). The underlying mechanisms remained to be defined. **Conclusion**: Adoptive immunity transfer from donor seemingly renders protective effect against HBV RS after allo-HSCT for patients with rHBV, which may influence future donor selection algorithm. cGVHD also has a higher risk of HBV RS. On the other hand, in a tertiary medical center with close monitor and prompt intervention, the adverse impact of HBV RS complication could possibly be reversed.

Disclosure of conflict of interest: None.

P746

Comparing Bayesian Cox Regression Model to Classical COX Regression Model in predicting overall mortality of Acute Leukemia patients who underwent Allogeneic Stem Cell Transplantation (HSCT): 954 cases

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Classical statistical approach philosophy depends on maximum likelihood and hypothesis testing to estimate regression parameters. In contrast, Bayesian approach incorporate prior knowledge to the observed data to estimate the posterior probability distributions using advanced sampling algorithms such as Markov chain Monte Carlo (MCMC) to estimate regression parameters. The superiority of Bayesian approach comes from its ability to formally incorporate prior knowledge into the analysis rather than using ad hoc adjustment of the results in situations where the result is not reasonable. This study aims to compare Bayesian and Classical proportional hazard regression model in predicting overall mortality using risk factors proposed by EBMT risk score model in Acute Leukemia patients underwent HSCT. Nine hundred fifty four patients transplanted between 1997 and 2013 were analyzed. Bayesian model was implemented using non-informative prior and MCMC algorithm. MCMC was implemented using 2500 burn-in and 40,000 iterations. Model diagnostics such as Trace plot and Autocorrelation plots were utilized to assess simulation accuracy. The proposed risk factors include age (<20, 20-40 and >40), donor recipient sex combination (male recipient, female donor vs. others), disease stage (early, intermediate, advance). However, donor type (HLA-identical sibling vs unrelated donor) was not included because more than 95% of the patients were HLA-identical. The estimated coefficients using Bayesian model were then compared to the estimated coefficients using Classical Cox model. Stratified probabilities of overall mortality were calculated based on a 5-point score model. Bayesian models were able to produce homogenous posterior distributions of the regression coefficients using MCMC. The Trace plots showed good mixing with Mean Square Error (MSE) and Autocorrelation plots converged to zero, figure (1). Patients with older age, advance disease have a higher risk of mortality. Female donor and time interval (from diagnosis to transplant) greater than one year, didn't affect overall mortality. Estimates using Bayesian COX model were in agreement with estimates using classical Cox model, table (1). Bayesian COX model provides a strong alternative to the classical COX model in estimating regression parameters. The superiority of Bayesian approach comes from its ability to incorporate prior knowledge that could be provided by the domain experts to the observed data. In this analysis, Bayesian COX model provided comparable estimates of regression coefficients to classical COX Model.

Disclosure of conflict of interest: The authors declared no conflicts of interest.

Table (1): Comparing Bayesian COX model to Classical COX model using risk factors proposed by EBMT risk score

Risk factors	*Bayesian COX model*		*Classical COX model*	
	AML	*ALL*	*AML*	*ALL*
Age				
<20	1	1	1	1
20-40	1.1	1.17	1.1	1.4
>40	1.23	1.6	1.28	1.2
Stage				
Early	1	1	1	1
Intermediate	1.82	1.9	1.87	1.9
Advance	2.16	3.5	2.3	3.6
Time interval, months				
<12	1	1	1	1
>12	0.61	0.82	0.6	0.81
Gender combination				
Others	1	1	1	1
RMDF	1.013	0.99	1.03	1.01
Risk score				
0-1	1	1	1	1
2-3	1.456	1.38	1.47	1.39
4-5	1.47	2.1	1.56	2.2

Table 1 [P745]

Table 1. Risk factors of HBV reactivation after Allo-HSCT

	Univariate HR (95% CI)	P	Multivariate HR (95% CI)	P
Age				
<50				
≧50	3.228 (1.45-7.21)	.0043*	2.004 (0.76-5.32)	.1628
Conditioning intensity				
Myeloablative				
Reduced intensity	3.070 (1.27-7.40)	.0125*	2.367(0.78-7.15)	.1268
Conditioning regimen				
Without ATG				
With ATG	0.858 (0.39-1.88)	.7016		
Exposed therapy				
Without Rituximab				
With Rituximab	0.791 (0.30-2.11)	.6399		
Stem cell				
BM				
PB	3.019 (0.40-22.54)	.2814		
Donor type				
Match sibling				
Others	0.932 (0.43-2.04)	.8595		
HLA-match				
Match				
Mismatch	1.275 (0.56-2.89)	.5607		
Acute GVHD				
None/grade 1				
Grade 2-4	1.163 (0.51-2.65)	.7203		
Chronic GVHD				
None				
limited/Extensive	11.429 (1.55-84.53)	.0170*	10.656 (1.44-78.86)	.0205*
Donor HBV profile				
Anti-HBs (-)				
Anti-HBs (+)	0.433 (0.20-0.95)	.0368*	0.359 (0.16-0.81)	.0138*
Anti-HBc (-)				
Anti-HBc (+)	0.719 (0.28-1.82)	.4867		

Figure 1 [P746]

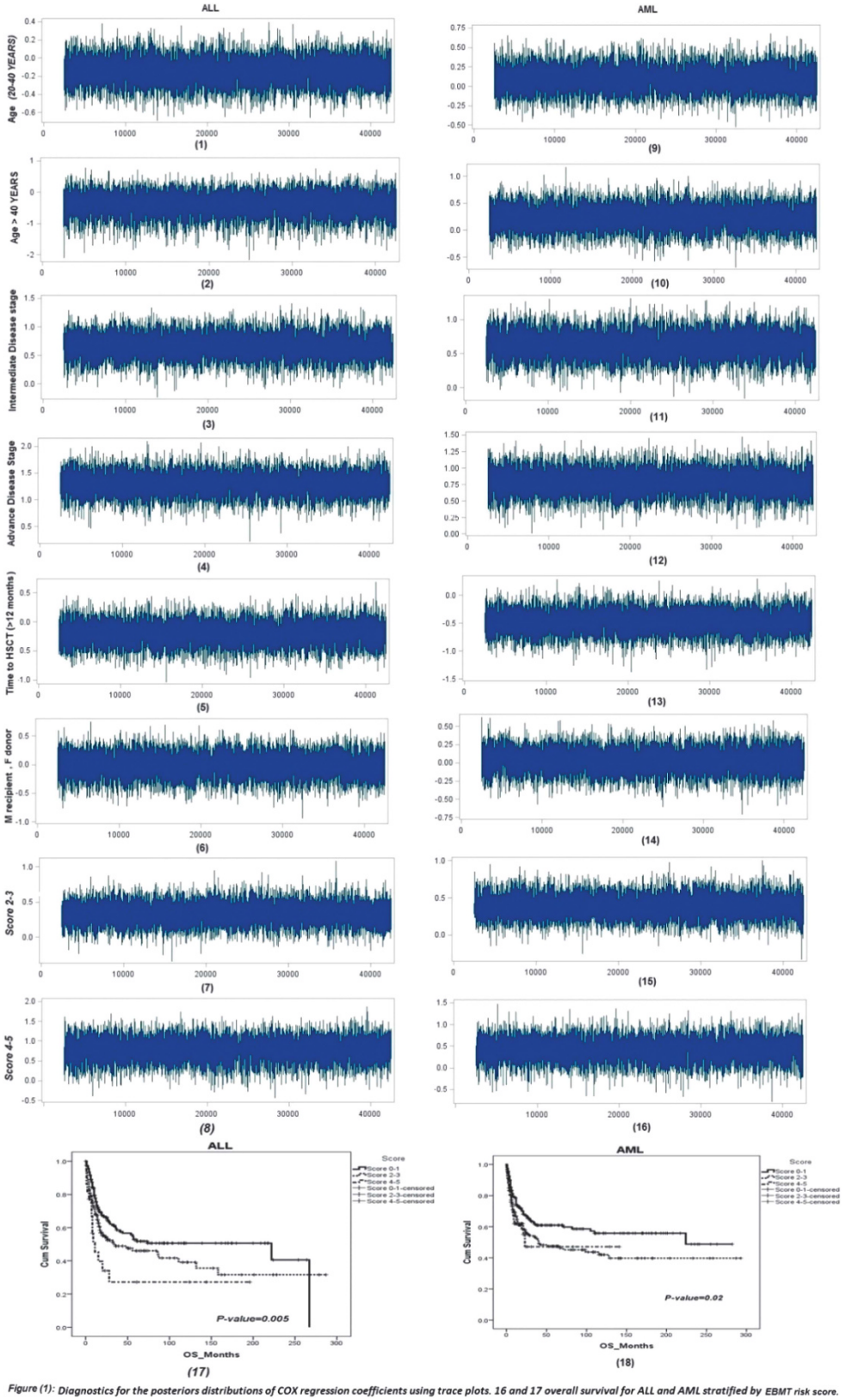

Figure (1): Diagnostics for the posteriors distributions of COX regression coefficients using trace plots. 16 and 17 overall survival for ALL and AML stratified by EBMT risk score.

P747
Previously published

P748
Previously published

P749
Modeling time-dependent effects for competing risks endpoints in allogenic stem cell transplantation—a piecewise constant approach

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Hematopoietic stem cell transplantation (HSCT) is a multifactorial process. Additional complexity is conferred by covariables showing time-dependent effects. We considered two competing risks situations and modeled the time dependent effects as piecewise-constant in different time periods after HSCT. 14951 patients from the German Registry for Stem Cell Transplantation diagnosed with acute myeloid leukemia, acute lymphocytic leukemia, myelodysplastic syndrome and non-Hodgkin lymphoma transplanted with peripheral blood stem cells (PBSCs) or bone marrow (BM) grafts were analyzed. This work is an extension of a previous study (see below). We extended the endpoints disease free survival (DFS) and overall survival (OS) to the competing risks settings: relapse, non-relapse mortality (NRM) as well as treatment related mortality (TRM), death from unknown causes and death from other causes (DOC). A multivariate Cox-regression model was fitted and tested for time-dependent effects. The standard Cox-model assumes constant effects (proportional hazard assumption – PHA) and calculates a time-averaged estimators when effects are time-varying. Instead, we computed an effect estimator before and after covariable-specific cutpoints in the Cox model. The cutpoints for the combined endpoints in Fuerst et al. also applied for competing risks endpoints and the PHA was satisfied. Patients with a poor Karnofsky performance score (KPS < 80) had a higher risk for TRM in the first 4 months compared to patients with a good KPS (HR 2.14, $P < 0.001$). Afterwards, the TRM-risk reduced to HR 1.32 ($P = 0.014$). Similar results for patients with poor KPS were found for the event relapse with the same cutpoint (first 4 months: HR 2.06, $P < 0.001$; afterwards HR 1.24 $P = 0.034$). The risk for relapse in patients treated with reduced intensity conditioning (RIC) compared to myeloablative conditioning (MAC) was constantly over time higher (PHA satisfied, HR 1.14, $P < 0.001$) but was time-dependent for the competing endpoint NRM: In the first 4 months, patients treated with RIC had a reduced NRM-risk (HR: 0.76, $P < 0.001$). Afterwards this effect was no longer detectable: HR 1.06, $P = 0.299$. A similar time dependent effect was observed for the events TRM and DOC (TRM: first 4 months: HR 0.79, $P < 0.001$, afterwards: HR 1.08, $P = 0.152$; DOC: first 4 months: HR 0.91, $P = 0.192$, afterwards: HR 1.11, $P = 0.021$). Graft source (PBSCs. vs BM) did not appear to affect the risk for relapse and DOC. However, for TRM and NRM, graft source exhibited a time dependent effect (TRM: first year HR 0.69, $P < 0.001$, after year 1 HR 1.46, $P = 0.019$; NRM: first 8 months HR 0.75, $P < 0.001$, afterwards HR 1.38, $P < 0.001$). Our approach provides more thorough insight into how diverse clinical predictors may impact endpoints of HSCT in a time-dependent manner. Extending the analysis for competing risks endpoints also made the identification of effects possible that would have remained unnoticed in standard Cox-regression models, e.g. graft source and its differential impact on NRM. In conclusion, our results provide insights for risk assessment and could aid in clinical decision-making.

Disclosure of conflict of interest: None.

Reference

1. Fuerst *et al. Haematologica* 2016; **101**(2): 241–247.