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ABSTRACTS COLLECTION

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Statistical Symposium Poster Session

P741.

Use of Variable Selection Methods to Identify Clinical and Immunological Factors Associated with the Clinical Outcome of Patients Following Allogeneic Hematopoietic Stem Cell Transplantation

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is used to treat a wide range of hematological disorders. However, the success of transplantation and the survival of patients can be compromised by clinical events such as relapse or graft-versus-host-disease (GVHD). While serum biomarkers have been studied in GVHD, multiparametric immunophenotyping has been less extensively explored and is associated with challenges in variable selection due to the large number of covariates. Here we demonstrate the utility of complementary statistical tools to identify clinical and immunological factors associated with the clinical outcome of patients following allo-HSCT.

Methods: We analyzed data from a previously reported phase 1-2 clinical trial evaluating the safety and efficacy of adding a CCR5 blockade to GVHD prophylaxis in allo-HSCT recipients [Reshef NEJM 2012, Moy Blood 2017]. We had access to flow cytometric immunophenotyping data from 37 patients (+/− CCR5 blockade treatment) on day 30 after transplantation. We focused on the time to the first event after transplant -- acute GVHD grade 2-4 (aGVHD24), chronic GVHD (cGVHD), or relapse. Patients were censored at the time of last follow-up or donor lymphocyte infusion (DLI). In this competing risk setting, we aimed to identify clinical and immunological factors associated with the different clinical outcomes. We used elastic-net penalization to select variables associated with the cause-specific hazards (the instantaneous rate of occurrence of each event among the patients still event-free) [Tapak Genomics Proteomics Bioinformatics 2015], and a boosting approach to select variables associated with the cumulative incidence functions (the expected proportion of patients experiencing each event over time) [Binder Bioinformatics 2009].

Results: Among the 37 patients, 17 experienced aGVHD24, 10 relapsed and 8 experienced cGVHD. 2 patients were censored at the time of DLI before any events happened. We identified factors associated with all clinical outcomes among more than 100 variables. In particular, CCR5 blockade treatment decreased both the hazard and the cumulative incidence of aGVHD24, and an increased number of $CD8^+$ $CCR5^+$ effector memory (EM) T cells at day 30 post-transplant was associated with a lower hazard of aGVHD24. We also found that higher numbers of $CD8^+$ $CD27^{neg}CD28^{neg}$ EM T cells were associated with a lower cumulative incidence of aGVHD24. Higher numbers of NK

$CD16^{hi}$ cells at day 30 were associated with a higher cumulative incidence of aGVHD24, but both a lower hazard and a lower incidence of relapse. Donor age was also positively associated with both a higher hazard and a higher cumulative incidence of relapse.

Conclusions: We developed a competing risk model to analyze data from patients who underwent allo-HSCT, using sophisticated methods for variable selection. Our results confirm the efficacy of the CCR5 blockade treatment in reducing the incidence of aGVHD24, and reveal that $CD8^+$ EM $CCR5^+$ cells are associated with a decreased hazard of aGVHD24. We also find evidence for a role of NK $CD16^{hi}$ cells in the balance between progression towards aGVHD24 or relapse.

Clinical Trial Registry: NCT00948753

Disclosure: Nothing to declare

P742.

Abstract already published.

P743.

Geographic and Socioeconomic Impacts on Survival Among Allogeneic Transplant Recipients

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Background: The Royal North Shore Hospital (RNSH), located 5.85 kilometres (kms) north of Sydney CBD, is a major tertiary referral for adult autologous and allogeneic transplants and a teaching hospital in Australia. The hospital receives referrals from within the northern regions of New South Wales and from other Australian states/territories. An audit was performed to analyse the impact of geographic location and socioeconomic status (SES) of transplant patients on survival. Previous analyses have been performed in other countries using the driving time from a patient address to a transplant centre and correlated the collected multiple patient SES variables with indices and predictors [1,2]. This audit, that has not been done in the Australian context, used actual distance between the recipient's and hospital address and the overall rank assigned by the Australian Bureau of Statistics (ABS) to postcodes.

Methods: A retrospective review of the transplant database was performed to identify patients receiving first allogeneic transplant between January 2011 and September 2019. Minimum follow-up was 100 days. The recipient's postcode at referral was used to obtain its equivalent classification on geographic and socioeconomic index (SEIFA) based on ABS data [3,4]. The association between geographic remoteness and SEIFA on recipient characteristics and transplant outcomes was assessed.

Results: 233 recipients were identified. Based on the remoteness structure classification, 84% (n = 196) of the recipients were from a major Australian city and 16% (n = 37) were from inner/outer regional Australia. The overall median postcode has a distance of 4.28 kms from RNSH with the closest recipient residing 809 metres and the farthest recipient living 3,145 kms away from RNSH. Looking at each group, the median city postcode is 12 kms from RNSH (range 0.8 – 260 kms) while the median regional postcode is 432 kms away from RNSH (range 30 – 3145 kms). Based on SEIFA, 58% (n = 136) were ranked as highly advantaged with national percentile rank between 91–100%; 23% (n = 54) received 51–90% national percentile rank; and 18% (n = 43) were from a least advantaged postcode with rank between 4–50%. AML was the most common indication for transplant among all groups and the most frequent age group was 31–60 years old. While recipients from major cities had numerically higher overall (OS) and progression-free (PFS) survival outcomes at all time-points compared the differences were not statistically significant (logrank chi2 = 0.79, p = 0.3744 on OS and logrank chi2 = 0.24, p = 0.6213 on PFS). OS based on SEIFA national rank has no significant impact (logrank chi2 = 0.03, p = 0.9836) with the least advantaged postcodes performing equally as those from the highly advantaged postcodes. PFS on SEIFA also provides no significant difference (logrank chi2 = 0.97, p = 0.6163). When SEIFA and remoteness classifications are combined, patients of a higher socioeconomic class (>51%) did better if they were from the city, while those of lower SEIFA group (<50%) had higher survival if they lived in a regional postcode.

Conclusions: We find no impact of remoteness or SES on outcome for recipients receiving an allogeneic transplant in our unit. Additional studies assessing remoteness and SES impacts at different post-transplant time points is planned.

Disclosure: Nothing to declare.