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732.ALLOGENEIC TRANSPLANTATION: DISEASE RESPONSE AND COMPARATIVE TREATMENT STUDIES

Impact of Multiple Minor Histocompatibility Antigen Differences on Graft-Versus-Host Disease and Relapse Risk in Pediatric Allogeneic Hematopoietic Cell Transplantation Recipients

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BACKGROUND Success of allogeneic hematopoietic cell transplantation (alloHCT) is sharped by alloreactivity, i.e. the ability of donor T-cells to recognize particular recipient motifs as non-self and get activated. Donor T-cells recognizing recipient tissue can cause harmful graft-versus-host disease (GvHD) while activity against leukemic blasts can protect against relapse (GvL). In HLA-matched alloHCT, alloreacticity is driven by subtle nonpathogenic variants in natural proteins, socalled minor histocompatibility antigens (miHAgs), however, not all variants are immunogenic. METHODS To analyze the impact of mHAgs-differences on alloHCT outcomes, we selected a purely pediatric cohort of 102 HLA-matched allo HCTs transplanted between 2003 and 2017. Panel sequencing of 46 validated miHAgs was performed using Ilumina MiSeq, only variants in the graft-versus-host direction were considered. RESULTS In a logistic regression model for the whole cohort acute GvHD incidence was significantly dependent on the proportion of miHAg mismatches (all genes) with an 95%-CI 1.0263-1.1998, p=.01 and an odds ratio of 1.1066. From all variants tested, only mismatches in TRIM42 were significant as a predictor with a FDR <.05. Furthermore, proportion of mismatches was a predictor of all-cause mortality. Risk of relapse was evaluated by regression analysis for competing risks: proportion of miHAg mismatches failed to be predictive for relapse (p=.37). However, looking at patients with acute lymphobastic leukemia (ALL) only (n=36), mismatches in hematopoiesis-restricted genes protected from relapse (95%-CI 1.0016-1.0712, p=.04, hazard ratio 1.0358). CONCLUSION Thus, in children GvHD and mortality seem to be related to the overall number of miHAg-differences whereas variants in hematopoiesis-restriced genes protect from ALL relapse. These data implicate that selection of TCRs with a specificity for hematopoietic miHAgs could be a way to improve GvL effect without increasing the risk of GvhD.

Disclosures Eyrich: *Vertex:* Membership on an entity's Board of Directors or advisory committees.

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