Classification of Donor KIR-Genotype Information to Predict Outcome after Unrelated Hematopoietic Stem Cell Transplantation: The Jury Is Still Out

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INTRODUCTION

Several studies suggest that harnessing natural killer (NK) cell reactivity could further improve outcome after allogeneic hematopoietic stem cell transplantation (alloHCT). Information on donor killer cell immunoglobulin-like receptor (KIR) genes might be instrumental for donor selection. A Receptor-Ligand model has been proposed which aims at augmenting donor NK-cell activation while minimizing inhibition. Information on education of KIR2DS1-positive NK cells (Venstrom et al., NEJM, 2012) and the predicted Receptor-Ligand interaction of KIR3DL1-positive NK cells (Boudreau et al., JCO, 2017) is utilized for this algorithm. By combining the information donors can be classified as KIR-advantageous or disadvantageous. Patients with donors, characterized by activating KIR2DS1 and weak/non-inhibiting KIR3DL1, were predicted to experience less relapse and improved survival compared to patients with donors, characterized by lacking an activating KIR2DS1 but presence of strong inhibiting KIR3DL1. This study aimed at validating this predictor in an independent cohort of patients.

METHODS

Donor samples were retrieved from the Collaborative Biobank (Dresden, Germany) and mapped to patient outcome data extracted from the German Registry for Stem Cell Transplantation. KIR typing was performed using a high resolution amplicon-based next generation sequencing method. KIR typing was performed using a modified disease risk index, performance status, donor age, HLA-match, sex match, CMV match, conditioning intensity, type of T-cell depletion and graft type.

RESULTS

The patient population was restricted to patients with AML or MDS. The whole cohort nor in subgroups of patients defined by conditioning intensity, HLA-compatibility, use of donor killer cell immunoglobulin-like receptor (KIR) genes might thus be instrumental for donor selection. A Receptor-Ligand model has been proposed which aims at augmenting donor NK-cell activation while minimizing inhibition. Information on education of KIR2DS1-positive NK cells (Venstrom et al., NEJM, 2012) and the predicted Receptor-Ligand interaction of KIR3DL1-positive NK cells (Boudreau et al., JCO, 2017) is utilized for this algorithm. By combining the information donors can be classified as KIR-advantageous or disadvantageous. Patients with donors, characterized by activating KIR2DS1 and weak/non-inhibiting KIR3DL1, were predicted to experience less relapse and improved survival compared to patients with donors, characterized by lacking an activating KIR2DS1 but presence of strong inhibiting KIR3DL1. This study aimed at validating this predictor in an independent cohort of patients.