GvHDHub

Interleukin-7 polymorphisms as predictors of GvHD and CMV

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Katrine Keilsen and colleagues of Copenhagen University Hospital Rigshospitalet in Denmark conducted a study correlating risk of adverse post-transplant outcomes with interleukin-7 (IL-7) polymorphisms. The findings were published in the February 2018 issue of Frontiers in Immunology.

IL-7 is integral for T-cell development in the thymus and peripheral T-cell homeostasis. The IL-7 receptor consists of a CD132 chain and an IL-7 receptor alpha chain (IL-7 Rα). Studies of the single nucleotide polymorphisms (SNPs) of IL-7 Rα have shown association with increased incidence of autoimmune inflammatory diseases and impact on timing of immune recovery in HIV patients. The aim of this study was to analyze transplant outcomes based on donor genotype of the rs6897932 SNP of IL-7 in allogeneic stem cell transplant patients.

Key Findings:

- N = 460 patients
- Median age = 26.3 years (0.3- 67 years)
    - Pediatric = 33.3%
    - Adult = 66.7%
- Donor type
    - Matched sibling = 31.9%
    - Matched unrelated = 53%
    - Mis-matched unrelated = 15%
- Stem cell source
    - Bone marrow = 71.5%
    - Peripheral blood = 28.5%
- Primary Disease
    - Hematologic malignancy/MDS = 74.8%
    - Other malignancy = 6%
    - Hematologic disorders = 19.1%
- Prep regimen
    - Total body irradiation + cyclophosphamide = 63.7%

    - Busulfan + cyclophosphamide = 23.3%
    - Another prep regimen = 13%
    - Anti-thymocyte globulin = 38.9%
- 90% of patients used cyclosporine + methotrexate for GvHD prophylaxis
- Genotypes
    - CC = 55.8%
    - CT = 38.7%
    - TT = 6.5%
- Overall incidence of acute GvHD (aGvHD) = 54.6%
- aGVHD risk
    - CT vs CC: CT HR = 2.02 (95% CI, 1.03-3.97), *P* = 0.040
    - TT vs CC: TT HR = 1.92 (95% CI, 0.63-5.07), *P* = 0.25
- Chronic GVHD (cGVHD) risk
    - CT vs CC: CT HR = 1.31 (95% CI, 0.87-1.97), *P* = 0.2
    - TT vs CC: TT HR = 1.99 (95% CI, 1.09-3.64), *P* = 0.025
- CMV infection
    - CT vs CC: CT HR = 1.3 (95% CI, 0.88-1.92), *P* = 0.19
    - TT vs CCL TT HR = 2.3 (955 CI, 1.24-4.27), *P* = 0.0083
- Overall survival (OS)
    - CT vs CC: CT HR = 1.65 (95% CI, 1.19-2.29), *P* = 0.0027
    - TT vs CC: TT HR = 0.9 (95% CI, 0.45-1.81), *P* = 0.77
- Transplant related mortality (TRM)
    - CT vs CC: CT HR = 2.28 (95% CI, 1.29-4.03), *P* = 0.0047
    - TT vs CC: TT HR = 0.56 (95% CI, 0.15-2.09), *P* = 0.39
- Relapse
    - CT vs CC: CT HR = 0.79 (95% CI, 0.46-1.34), *P* = 0.38
    - TT vs CC: TT HR = 0.43 (95% CI, 0.12-1.47), *P* = 0.18

This study reviewed the correlation of transplant related outcomes to donor IL-7 genotypes. In general, patients who were homozygous or heterozygous for the T allele, had adverse results in several outcome measures, compared to those homozygous for the C allele. Heterozygosity of the T allele lead to an increase in aGVHD and TRM, in addition to decreased OS. Heterozygous TT donor products lead to an increase in cGVHD and CMV infections. This data is useful for consideration of donor genotype testing pre-transplant, to help improve patient outcomes.

References

1. Kielsen K. *et al.* Donor Genotype in the Interleukin-7 Receptor α-Chain Predicts Risk of Graft-versus-Host Disease and Cytomegalovirus Infection after Allogeneic Hematopoietic Stem Cell Transplantation. Front Immunol. 2018 Feb 2. DOI: 10.3389/fimmu.2018.00109.