Update on Comparative Analysis of Immune Reconstitution in HIV-Positive Recipients of Allogeneic and Autologous Stem Cell Transplant on the BMT CTN 0903/AMC-080 and BMT CTN 0803/AMC-071 trials

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Statement of the Problem: HIV-positive (HIV(+)) individuals demonstrate chronic changes in cellular immunity, including depletion of CD4+ T cells, elevation in CD8+ T cells, increased markers of senescence and activation. We hypothesized that HIV profoundly impacts immune reconstitution after treatment of hematologic malignancies. We performed a detailed assessment of immune reconstitution in HIV(+) recipients of autologous (auto-SCT) and allogeneic (allo-SCT) hematopoietic stem cell transplant on the BMT CTN 0803/AMC 071 (n=38) and BMT CTN 0903/AMC (n=17) prospective clinical trials. These were compared to HIV(-) auto-SCT recipients (n=30) and healthy controls (n=71).

Methodology & Theoretical Orientation: 5-color flow cytometry of whole blood was performed at days 56, 180 and 365 post-transplant (transplant-recipient cohorts) or at a single time point (healthy controls). Results were analyzed by principal component analysis (PCA), Wilcoxon rank-sum test and feature importance score analysis (FIS).

Findings: PCA showed that HIV(+) auto-SCT and allo-SCT recipient immune profiles segregated together and away from HIV(-) auto-SCT recipients and healthy controls. HIV(+) auto-SCT and allo-SCT recipients showed significant differences in 38 and 60 immune cell populations compared to healthy controls on day 56, and 39 and 55 immune cell populations at day 365 post-transplant, respectively ($p<0.031$). In contrast, 7 immune cell populations were identified as significantly different between HIV(+) auto- and allo-SCT recipients on day 56, and none at 1 year post-transplant ($p<0.031$). FIS identified activated T cells, cytotoxic T cells (total, naïve, memory, effector higher in HIV(+) cohorts), and naïve, central and effector memory T helper subsets (lower in HIV(+) cohorts) as significantly impacting the difference between HIV(+) cohorts and healthy controls.

Conclusion & Significance: HIV(+) auto-SCT and allo-SCT recipients demonstrate features of immune activation and converging immune reconstitution trajectories during the post-transplant year, distinct from HIV(-) auto-SCT recipients and healthy controls, suggesting that controlled HIV status significantly impacts post-SCT immune reconstitution. Clinical significance of these findings requires further study.

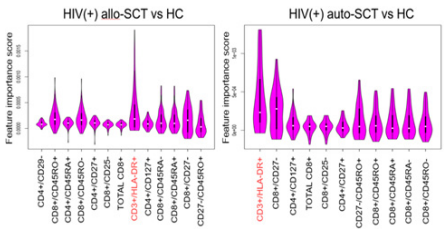

Figure 1. Feature importance score analysis identified immune cell populations with the highest impact on the differences between HIV(+) stem cell transplant recipients and healthy controls (HC) at 1 year post-transplant.

Biography

Shindiapina is an Assistant Professor at the Division of Hematology, Department of Internal Medicine at the Ohio State University, OH, USA. Dr. Shindiapina is a member of the translational lymphoma research group, together with Dr. Robert Baiocchi. Dr. Shindiapina's laboratory focuses on immune reconstitution studies in immunocompromised patients with hematologic malignancies and virus-driven lymphomas. Dr. Shindiapina and Dr. Baiocchi are members of the AIDS Malignancy Consortium.

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