Using CMV -QuantiFERON Assay to Assess CMV Specific Immune Reconstitution in Early Post Hematopoietic Stem Cell Transplant (HSCT) Phase

Alka Khadwal¹, Suresh Selvam¹, Kapil Goel², Mini Singh³, Gaurav Prakash¹, Deepesh Lad¹, Manupdesh Sachdeva³, Neelam Varma³ and Pankaj Malhotra¹

¹Clinical Hematology & BMT unit, Department of Internal Medicine, Post Graduate Institute of Medical Education & Research, Chandigarh, India
²Department of Virology, Post Graduate Institute of Medical Education & Research, Chandigarh, India
³Department of Laboratory Hematology, Post graduate Institute of Medical Education & Research, India

Background: HSCT are increasingly performed worldwide with the curative intent for the many malignant and non-malignant diseases but are associated with immunocompromised state for variable period and delayed antiviral T cell immune reconstitution. CMV reactivation can result in significant morbidity as well as mortality. Acquisition of CMV specific cellular immunity can be assessed using CMV -QuantiFERON assay which measures amount of interferon-gamma secreted from CMV-specific T-cells in response to stimulation by CMV proteins.

Materials and Method: We prospectively studied anti CMV CD8 + T cell immunity using QuantiFERON-CMV assay in five consecutive allogeneic HSCT recipients during first 100 days post HSCT. Serological status of patients and donors at base line were determined using commercially available ELISA kit. CMV DNA copy numbers were assessed weekly post HSCT on a fully automated platform - Cobas Ampliprep and TaqMan 48 (Roche, USA). CMV QuantiFERON kits were used to quantify IFN-gamma in blood samples collected at baseline, day +28, +56 and +100.

Results: We prospectively studied the immune reconstitution against CMV during initial 3 months of posttransplant phase in five consecutive allogeneic HSCT (AML=2, ALL=1, AA=2). Mean age was 18 years and all were male. Pretransplant, all patients and the donors were seropositive for CMV. CMV reactivation was seen in all 5 allogeneic HSCT recipients (Haplo=2 & MSD=3) at median 24 days post-transplant. At D+28 and D+56, CMV specific T cell immunity, as measured by CMV QuantiFERON assay, was indeterminate / absent immunity in all five cases and by D+100, two cases had acquired anti CMV specific immune response. Two allogeneic -HSCT (1 ALL and 1 AML) who developed acute GVHD, continued to have indeterminate reactivity and had high CMV viral copies/ml (maximum-30,400 and 94,300 respectively) requiring ganciclovir therapy while two cases who became CMV-QuantiFERON positive had lesser rise in CMV viral copies (up to 150 cps/ml) and cleared spontaneously. One case remained non-reactive with maximum CMV DNA copies up to 2200 and died at D+76 despite receiving anti-CMV therapy.

Conclusion: This small case series showed that CMV reactivation occurred by third week and in the absence of acute GVHD, CMV specific T cell immunity started appearing by third month post HSCT. Those with positive CMV-QuantiFERON assay had less viral load and cleared virus spontaneously viza-viz those with indeterminate/nonreactive results who can accumulate significant viral copies numbers warranting CMV specific therapy.

Keywords: Anti-CMV CD+T cells , CMV-QuantiFERON, HSCT