Allogenic haematopoietic stem cell transplantation with post-transplant cyclophosphamide: incidence, risk factors and mortality of double-stranded DNA viral infections

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Background: we estimated the incidence of viral infections [VI: Cytomegalovirus (CMV), adenovirus (ADV), human herpes virus-6 (HHV6) and BK-polyomavirus hemorrhagic cystitis (BKPyV-HC)], their predictive factors and the incidence of infection-related mortality (IRM) after allogenic hematopoietic cell transplantation (HCT) with Graft-versus-Host Disease (GVHD) prophylaxis based on post-transplant cyclophosphamide (PT-Cy).

Materials/methods: cohort study on adults who underwent HCT with PT-Cy platform, from January 2013 to December 2017. The Fine-Gray competing risk model was applied to estimate the cumulative incidence function (CIF) of ≥1 VI (first occurrence among CMV, ADV, HHV6, BKPyV-HC) and their predictive factors.

Results: We analyzed 235 patients with a median age of 50 years (IQR=37-62): 62%, 21% and 17% received haploidentical, matched-unrelated donor (MUD) and matched-related donor (MRD) transplantation, respectively. Acute-GVHD grade≥2 occurred in 32% of patients. During 14739 days of follow-up, 208/235 patients experienced ≥1 VI after a median of 20 days (IQR=16-26): the estimated 90-day CIF was 91% (95%CI=86%-94%) and was significantly lower in MRD (Figure1). CMV and HHV6 reactivation occurred in 144(61%) [14% end-organ disease; median time to CMV: 34 days (IQR=19-54)] and 179(76%) patients [8% cutaneous rash/delayed engraftment; 14% end-organ disease; median time to HHV6: 24 days (IQR=19-26)], respectively. BKPyV-HC and ADV infection developed in 36(15%) [median time to BKPyV-HC: 32 days (IQR=14-45)] and 14(6%) patients [57% end-organ disease; median time to ADV: 50 days (IQR=18-86)], respectively. By multivariate analysis, after adjustment for age, sex, year of HCT, the CIF of ≥1 VI was higher in patients with acute-GVHD grade≥2 [adjusted hazard ratio (AHR)=1.32, 95%CI=1.01-1.74], who received haploidentical [AHR=2.00, 95%CI=1.37-3.12] or MUD [AHR=2.04, 95%CI=1.29-3.21] transplantation and in host/donor CMV-serology mismatch [pos/pos vs neg/neg: AHR=2.95, 95%CI=1.55-5.63; pos/neg vs neg/neg: AHR=2.41, 95%CI=1.23-4.73; neg/pos vs neg/neg: AHR=2.35, 95%CI=1.07-5.19]. The four-month IRM CIF was 3%, 4% and 10% in MRD, MUD and haploidentical transplantation, respectively (Gray’s test: p=0.106).

Conclusions: with PT-Cy platform, we observed a high incidence of ≥1 VI within early post-engraftment phase, mainly CMV and HHV6 infections; however, end-organ diseases were low and IRM did not exceed 10%. Factors associated with the occurrence of ≥1 VI were haploidentical and MUD setting, acute-GVHD grade≥2 and unfavorable host/donor CMV-serology.