





Blood 142 (2023) 6984-6985

The 65th ASH Annual Meeting Abstracts

## **ONLINE PUBLICATION ONLY**

## 721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

## Role of Polyomavirus BK and Adenovirus in the Development of Urinary Tract Complications in Pediatric Hematopoietic Stem Cell Transplantation

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One of the major challenges in pediatric hematopoietic stem cell transplantation (HSCT) is the susceptibility to viral infections and reactivations that can lead to potentially life-threatening complications and increase the transplant-related mortality (TRM). Polyomavirus BK (BKPyV) and Adenovirus (AdV) represent the predominant causes of urinary tract complications, in particular hemorrhagic cystitis (HC), in HSCT recipients. Treatment options for BKPyV and AdV infections are limited and there is no accepted standard of care for the prevention and treatment of these HSCT complications. The aim of our retrospective study was to analyze the incidence of BKPyV and AdV infection in urinary and plasma samples of pediatric patients undergoing HSCT for both malignant and non-malignant disease at a single pediatric Hematology-Oncology unit. Endpoints were the cumulative incidence of infection, measured on blood and urine samples, in the first 100 days after HSCT, prevalence of asymptomatic and symptomatic infection, and correlation between BKPyV and AdV DNAemia and DNAuria and the development of HC. A total of 79 patients were analyzed. Thirty-seven (47%) patients were positive for BKPyV on urine samples and 20 (30%) on blood samples within the first 30 days after transplantation. As for AdV, 11 (9%) patients were positive on urine samples and 18 (15%) on blood samples.

In our pediatric cohort, BKPyV DNAuria was a frequent event after HSCT, while BKPyV DNAemia was observed less frequently, and was accompanied by higher viruria values (p-value <0,001, with a median viral load in the urine of 3.8 x 10 <sup>9</sup> copies/mL). Conversely, AdV positivity in urine is rare, while AdV DNAemia was more frequent, due to the modality of BKPyV and AdV distribution (urothelium is the main reservoir for BKPyV, while intestinal lymphocytes represents the main reservoir for AdV). Of the 37 patients with BKPyV DNA on urine samples, 11 (30%) developed a symptomatic infection with grade II (5 patients, 40%) and grade III (6 patients, 60%) HC. We did not observe any correlation between BKPyV DNA urinary levels and the development of HC, as higher viral loads have not been shown to be good predictors of occurrence or severity of HC. Cumulative incidence (CI) of BKPyV infection was higher in haploidentical HSCT (51%) and matched unrelated donors (MUD) (48%) than in HSCT from matched familiar donors (31%). Similarly, CI of AdV reactivation was higher in haploidentical HSCT (16%) than MUD (6%) and matched familiar donors (9%). Choice of donor, the type of immunosuppression used and the intensity of conditioning regimen represented predictors of both blood and urine DNA positivity for both viruses. In our cohort, positivity for BKPyV on blood and/or urine did not increase the risk of transplant-related mortality and did not affect the overall survival after HSCT.

On the basis of our data, we now perform screening of BKPyV viruria only in symptomatic patients or in transplant recipients with specific risk factors (type of donor, severity of immunosuppression). Similarly, search for BKPyV DNAemia is reserved to subjects with a high viral load on urine. Likewise, search for AdV on urine samples is performed on symptomatic patients with high-load AdV DNAemia.

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**Disclosures** No relevant conflicts of interest to declare.

https://doi.org/10.1182/blood-2023-187768