

# Hemorrhagic Cystitis after Allogeneic Hematopoietic Stem Cell Transplantation in Acute Myeloid Leukemia Patients

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## Introduction

- **Hemorrhagic cystitis (HC) after hematopoietic stem cell transplantation (HSCT)**
  - one of the serious complications in allogeneic HSCT recipients
  - suggested pathogenesis
    - urothelial damage due to myeloablative conditioning
    - reactivation of virus, especially BK polyomavirus (**BKPyV**)
  - There are limited data for incidence, clinical characteristics, and outcome of HSCT recipients with HC as well as effective treatment option.

## Aim

This study aimed to identify

- 1) disease burden of HC after HSCT
- 2) potential risk factors of HC
- 3) characteristics of HC/BKPyV-HC developed after HSCT
- 4) outcome of HC patients

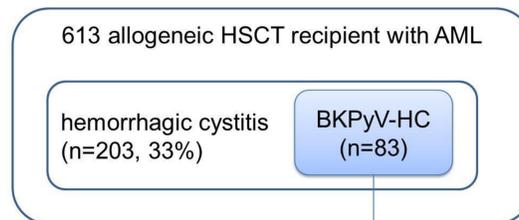
## Methods

- **Retrospective chart review**
- **Study subjects.**
  - all consecutive allogeneic HSCTs between Jun. 2012 – Jan. 2018
  - in adult acute myeloid leukemia (AML) cohort at the Catholic Hematology Hospital, Seoul St. Mary's Hospital
- **Definitions of HC: 1)** clinically significant hematuria, **2)** along with dysuria and/or lower abdominal pain.
- **The severity of hematuria** was described as microscopic (grade 1), macroscopic (grade 2), macroscopic with clots (grade 3), macroscopic with clots and postrenal failure secondary to urinary tract obstruction (grade 4).
- **Triad of diagnostic criteria for BKPyV-HC**
  - 1) Clinical symptoms and/or signs of cystitis, such as dysuria and lower abdominal pain
  - 2) hematuria grade 2 or higher
  - 3) Urine BKPyV  $\geq 7$  Log<sub>10</sub> copies/mL

## Results

### [HC after HSCT]

- A total of 613 allogeneic HSCT recipient with AML were included.



• grade 2 (n=15), grade 3 (n=41), grade 4 (n=27)

Figure 1. Development of hemorrhagic cystitis

- HC was developed in 33.1% of patients (n=203).

### [Causative virus and HC]

- BKPyV (n=83) was the most common cause of HC (13.5%), followed by JC virus (n=35) and adenovirus (n=9).
- Time to HC diagnosis after HSCT
  - BKPyV-HC : median 31 days (range, 2–742)
  - adenovirus-HC : median 99 days (range, 13–783)

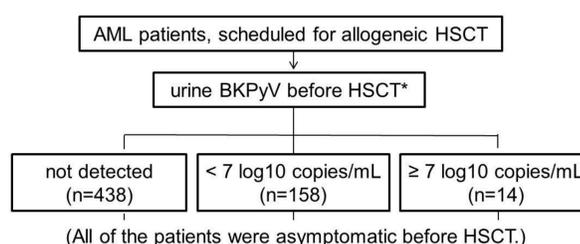
### [Characteristics of patients between BKPyV-HC vs. others]

Table 1. Demographics between BKPyV-HC and control

	Control (n=530)	BKPyV-HC (n=83)	p
Age	45.9	46.4	0.404
Male	288 (54.3%)	44 (53.0%)	0.821
Donor types			
MSD	241 (45.5%)	19 (22.9)	<0.001
haploidentical	144 (27.2%)	42 (50.6)	
MUD	145 (27.4%)	22 (26.5)	
Acute GVHD	283 (53.4%)	47 (56.6%)	0.583
Chronic GVHD	298 (56.2%)	45 (54.2%)	0.732
Steroid use	149 (28.3%)	22 (27.2%)	0.828
Overall death	182 (34.3%)	42 (50.6%)	0.004

Abbreviations. GVHD, graft-versus-host disease; MSD, matched sibling donor; MUD, matched unrelated donor

### [pre-HSCT urine BKPyV reactivation]



<after HSCT>	Control (n=530)	BKPyV-HC (n=83)	p
any hematuria	284 (64.8%)	113 (71.5%)	9 (64.3%)
HC	136 (31.1%)	60 (38.0%)	6 (42.9%)
BKPyV-HC†	33 (7.5%)	45 (28.5%)	4 (28.6%)

†p<0.001

Figure 2. Flow chart grouped by pre-HSCT urine BKPyV level

## Results (cont')

### [Peak Viral load of BKPyV-HC]

- Peak level of BKPyV after HSCT
  - Urine: median 9.52 Log<sub>10</sub> (range 7.01–11.32 Log<sub>10</sub>) copies/mL
  - Blood: median 3.27 Log<sub>10</sub> (range 0–7.34 Log<sub>10</sub>) copies/mL

### [Treatment and outcomes]

- The administration of cidofovir was performed in only 22 cases
  - BKPyV-HC unresponsive to supportive treatment
  - adenovirus-HC
- There was no significant difference in the survival rates between cidofovir and non-cidofovir group.
- **Mortality** was significantly higher in BKPyV-HC group than control group (50.6% vs. 34.3%, p=0.004), as well as HC vs. others (57.1% vs. 26.3%, p<0.001) in this cohort.

## Conclusions

- HC is a common infectious complication that occurs in about 33% of AML patients after HSCT.
- The major causative virus is BKPyV and BKPyV-HC occurs in 13.5% of AML patients after HSCT.
- Haploidentical or unrelated donor transplantation increases risk of HC.
- Asymptomatic BKPyV detection from urine before HSCT also increases risk of post-HSCT BKPyV-HC.
- Overall mortality is significantly higher when HC is complicated.
- Treatment options are still limited, largely focused on supportive care such as intravenous hydration, continuous irrigation of bladder, transfusion, etc.
- Further prospective studies are needed to elucidate the role of cidofovir with selective indications considering the outcome of patients.

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