Characterization of Antiviral Prescribing Practices for Cytomegalovirus Following Adult Hematopoietic Stem Cell Transplant in BC

Kate Butcher, B.Sc.(Pharm); Katie Lacaria, B.Sc.(Pharm), ACPR; Stephanie Garland, B.Sc.(Pharm), ACPR; Alissa Wright, MD; Allison Mah, MD; Tim TY Lau, PharmD; Nilu Partovi, PharmD; Marthe Charles, MD; Christopher Lowe, M.Sc., MD, FRCPC

Background

- Cytomegalovirus is a serious infectious complication of hematopoietic stem cell transplantation (HSCT) with a reported incidence of 35 – 70%
- CMV replication detected in the blood (viremia) is a risk factor for CMV disease
- Pre-emptive antiviral therapy, consisting of the administration of antiviral drug upon detection of CMV viremia, is a strategy to reduce CMV disease
- First-line therapy is ganciclovir or its pro-drug valganciclovir
- Second-line therapy with foscarnet is reserved for ganciclovir-induced neutropenia or CMV resistance
- True CMV resistance following HSCT is low, especially in patients that have not been exposed to the antiviral
- Current practice of CMV treatment and utilization of antiviral therapy is unknown among adults HSCT recipients in BC

Objectives

- Determine the incidence of CMV infection within 100 days following HSCT
- Characterize prescribing practices for pre-emptive antiviral therapy following HSCT

Methods

- Design: Single-centre retrospective chart review
- Data source: BMTserv database, PCIS database, paper charts
- Study dates: June 12, 2015 to June 12, 2017
- Inclusion: Adult, allogeneic HSCT recipients with detectable CMV DNA titer within 100 days following HSCT
- Exclusion: >1 HSCT within 100 days
- Analysis: descriptive statistics

Results

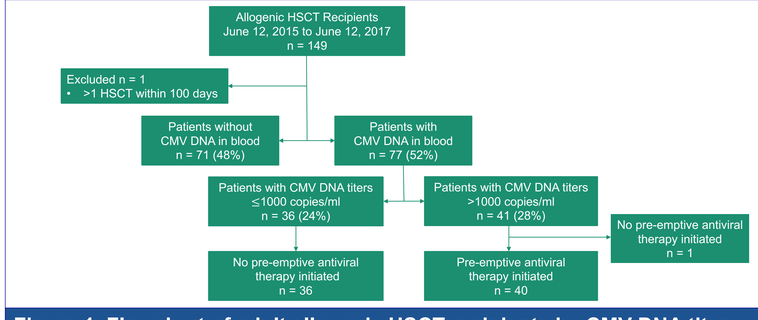

Figure 1. Flowchart of adult allogenic HSCT recipients by CMV DNA titer.

Table 1. Demographics of patients that received pre-emptive antiviral therapy.

Characteristic		n = 40 (%)
Age (years, IQR)		47 (39–58)
CMV serostatus (recipient/donor)	+/+	19 (47.5)
	+/-	19 (47.5)
	-/+	2 (5)
HLA type	Matched, related	7 (17.5)
	Matched, unrelated	22 (55)
	Mismatched, unrelated	6 (15)
	Haploidentical	5 (12.5)
Conditioning regimen	Myeloablative	30 (75)
	Nonmyeloablative	2 (5)
	Reduced-intensity	8 (20)
	ATG conditioning	14 (35)
Steroid dose	Steroids <1mg/kg	14 (35)
	Steroids ≥1mg/kg	26 (65)
Acute GVHD grade	No acute GVHD	10 (25)
	I	6 (15)
	II	15 (37.5)
	III	8 (20)
	V	1 (2.5)

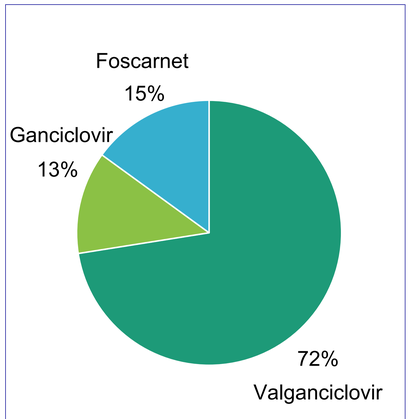

Figure 2. Initial antiviral prescribed for pre-emptive therapy. The main rationale for foscarnet use was neutropenia at the start of therapy.

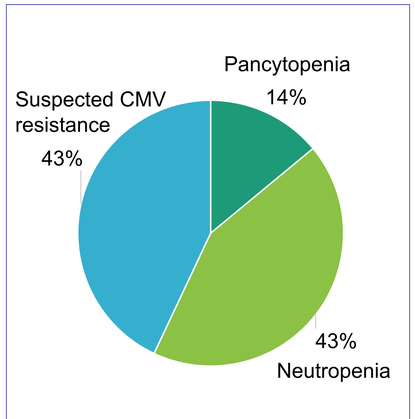

Figure 3. Rationale for change from initial therapy to foscarnet in 7 (21%) of the 33 patients initially prescribed ganciclovir or valganciclovir.

Table 2. G-CSF prescribing practices in patients that received ganciclovir or valganciclovir therapy.

G-CSF prescribing variable	n = 33 (%) or median (IQR)
Proportion of patients that received G-CSF	9 (27)
Number of G-CSF doses received	4 (3, 6)
Neutrophil count at G-CSF initiation	0.6 x 10^9/L (0.5, 0.6)

Additional Results

- Of the 3 patients changed from initial therapy with ganciclovir or valganciclovir to foscarnet for suspected CMV resistance, 2 patients (67%) had resistance testing performed
- No patients had CMV resistance identified
- Patients received a median duration of 14 days (IQR 13.5 – 15.5) ganciclovir and/or valganciclovir prior to the change to foscarnet
- The median time to peak CMV DNA titer after initiation of antiviral therapy for these patients was 13 days (IQR 12 – 13.5)
- Overall, the median time to peak CMV DNA titer after initiation of antiviral therapy was 7 days (IQR 2 – 11)

Limitations

- Risk of CMV infection persists beyond 100 days following HSCT; therefore, infection and prescribing patterns described only reflect those within the early period following HSCT
- Antiviral use captured does not reflect total treatment course
- Retrospective design is reliant on accurate documentation

Conclusions

- Incidence of CMV following HSCT in BC is consistent with published rates
- Initial pre-emptive antiviral therapy is appropriate
- Earlier initiation of G-CSF may be considered to manage ganciclovir-induced neutropenia and reduce foscarnet use
- Change in therapy to foscarnet for suspected resistance should be considered after 21 days of initial ganciclovir or valganciclovir therapy
- Future research is needed to assess the impact of earlier initiation of pre-emptive therapy and the role of novel prophylactic therapy