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Joanne Reekie
Blegdamsvej 9, 2100 Copenhagen, Denmark
Tel: +45 35 45 58 56
Email: joanne.reekie@regionh.dk

MATCH
Management of Post-Transplant Infections in Collaborating Hospitals

Absolute Lymphocyte Count as a Predictor of Cytomegalovirus Infection and Recurrence in Hematopoietic Stem Cell Transplant Recipients

J Reekie[1], M Helleberg[1], C Ekenberg[1], MP Khurana[1], IP Lodding[1], A Mocroft[2], JD Lundgren[1], H Sengeløv[3] for the MATCH study group

[1]Centre of Excellence for Health, Immunity and Infections (CHIP), Department of Infectious Diseases, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark, [2]Institute for Global Health, Infection and Population Health, University College of London (UCL), London, United Kingdom, [3]Department of Haematology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

BACKGROUND

- Cytomegalovirus (CMV) infection is a serious complication following hematopoietic stem cell transplantation (HSCT)
- CMV can lead to serious end organ disease and is associated with higher rates of infections, graft loss, morbidity and mortality
- Absolute lymphocyte count (ALC) is a relatively inexpensive and readily available marker of host immunity that could help predict CMV infection and relapse

AIM

- To investigate the association between ALC and CMV infection and recurrence in HSCT recipients

OUTCOMES

- **First CMV infection:** The first of two-consecutive plasma CMV PCR ≥273 IU/mL taken ≤14 days of each other, or one CMV PCR ≥2730 IU/mL in the year after transplant
- **Recurrent CMV:** A second diagnosis of CMV infection within 6 months of clearing and stopping treatment for the first CMV infection. Clearance of CMV was defined as the first date of two consecutive negative CMV PCR tests.

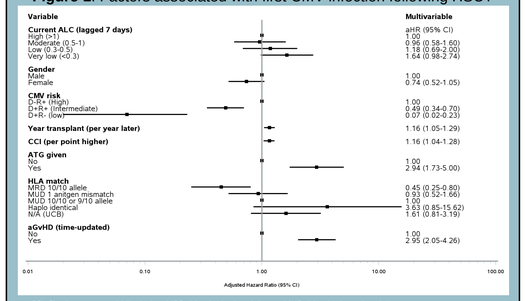
METHODS

- All adults (≥18 years) who underwent a HSCT at Rigshospitalet, Denmark, between 2011 – 2016 were included
- Patients with unknown (n=35) or D-R- (n=100) CMV IgG serostatus at transplant were excluded
- Cox regression analysis was used to investigate risk factors, including ALC for CMV infection and recurrence
- ALC was investigated as a time-updated risk factor lagged by 7 days for the first episode of CMV infection
- For recurrent CMV ALC at the time of stopping treatment for the first CMV infection (+/- 7 days) was investigated.

Table 1: HSCT recipient demographics at transplant

		All HSCT recipients N=352		Assessed for recurrent CMV N=102	
Male (n, %)		202	57.4	68	66.67
Myeloablative Conditioning (n,%)		142	40.3	42	41.2
CMV IgG serostatus (n,%)	D-R+ (High)	149	42.3	62	60.78
	D+R+ (Intermediate)	163	46.3	38	37.25
	D+R- (low)	40	11.4	2	1.96
ATG given (n,%)		36	10.2	10	9.8
HLA match (n,%)	MRD 10/10 allele	72	20.5	9	8.82
	MUD 1 antigen mismatch	33	9.4	9	8.82
	MUD 10/10 or 9/10 allele	222	63.1	76	74.51
	Haplo identical	2	0.6	2	1.96
	N/A (Umbilical Cord Blood)	23	6.5	6	5.88
Age (median, IQR)		56	43-63	52	43-62
Year of transplant (median, IQR)		2014	2012-2015	2014	2013-2015

Figure 1: Factors associated with first CMV infection following HSCT



CCI: Charlson commorbidity Index, MRD: Matched related donor, MUD: Matched unrelated donor

Figure 2: Cumulative incidence of recurrent CMV, stratified by ALC at stopping treatment for first CMV infection

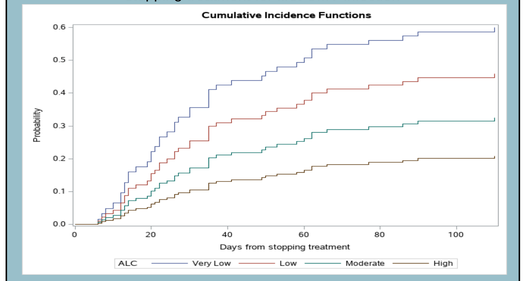


Table 2 Characteristics of the first two CMV infection episodes after HSCT

	First CMV infection		CMV recurrence	
Total assessed for outcome (N, %)	**352**	**100**	**102**	**100**
CMV infection (N, % of total)	**143**	**40.6**	**41**	**41.0**
CMV viral load at detection, IU/ml (median, IQR)	419	273-883	564	273-1456
Days from baseline to CMV infection (median, IQR)	49	35-66	27	16-50
Cleared infection (N, % with infection)	**131**	**91.6**	**35**	**85.4**
Days from detection of CMV infection to clearance (median , IQR)	24	18-32	25	20-33
Maximum CMV viral load, IU/ml (median, IQR)	1365	682-3144	1092	701-2912
CMV Treatment record (N. % cleared infection)	**113**	**86.2**	**31**	**88.6**
Days from detection to treatment initiation (median, IQR)	3	2-6	3	1-6
Days receiving CMV treatment (median, IQR)	38	28-51	32	27-28

Figure 3: Factors associated with recurrent CMV

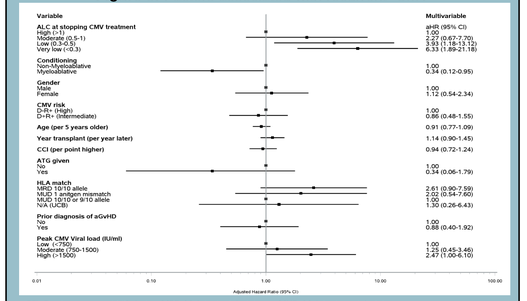


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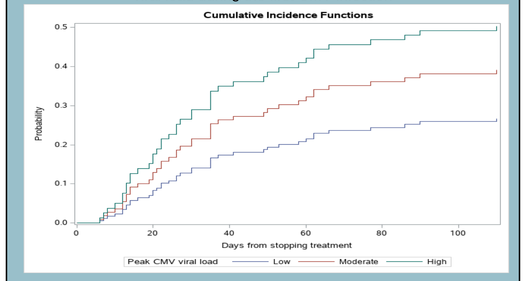
Figure 4: Cumulative incidence of recurrent CMV, stratified by peak CMV viral load during the first CMV infection



RESULTS

First CMV infection

- 352 HSCT recipients were included (Table 1), with 143 (40.6%%, 95%CI 35.4%-45.9%,) experiencing an episode of CMV DNAemia in the first year post transplant (Table 2)
- A lower ALC was associated with a higher risk of CMV infection in univariate analysis but was attenuated after adjusting for other factors in the multivariable model, particularly aGVHD (Figure 1)

Recurrent CMV

- 102 HSCT recipients were investigated for risk of recurrent CMV of which, 41 (40.2%, 95%CI 30.6%-50.4%) had a recurrent CMV episode (Table 2)
- The risk of recurrent CMV infection in the first 90 days after stopping pre-emptive CMV prophylaxis was estimated to be 20% (95% CI 8%-47%) in those with high ACL (>1 x10^9/L) compared to 60% (95%CI 42%-85%) in those with very low ALC (≤0.3 x10^9/L) (Figure 2)
- HSCT recipients with a very low ALC (≤0.3 x10^9/L) were more than six times as likely to experience recurrent CMV in following 6 months (HR 6.33, 955%CI 1.89-21.18) compared to those with a high ALC (>1 x10^9/L) after adjusting for other factors (Figure 3)
- A higher peak CMV viral load during the first episode of CMV infection was also associated with an increased risk of recurrent CMV infection (Figure 4).
- In adjusted analysis a high peak viral load (>1500 IU/ml) was associated with a 2.47 times higher risk of recurrent CMV (95%CI 1.00-6.10) than a low peak CMV (<750 IU/mL) (Figure 3)

CONCLUSIONS

- A lower ALC at the time of stopping treatment for the first CMV infection was associated with an increased risk of recurrent CMV
- ALC could be used to help guide decisions for augmented CMV surveillance and clinical awareness of CMV disease symptoms in these patients.

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