Conclusion

Results of Post Cytomegalovirus (CMV) Prophylaxis Surveillance in High Risk Lung and Heart Transplant Recipients

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Introduction

- Late onset cytomegalovirus (CMV) is a major cause of morbidity in high risk (D+/R-) solid organ transplant recipients, particularly lung and heart transplant recipients.
- The optimal monitoring strategy post prophylaxis cessation is unknown
- Surveillance with pre-emptive treatment post prophylaxis may halt the progression to CMV disease and reduce CMV related hospitalizations

Objectives

- To assess the efficacy of post CMV prophylaxis surveillance strategy in preventing late CMV disease in D+/R- lung transplant recipients (LTRs) and heart transplant recipients (HTRs)
- To assess the rate of CMV related hospitalizations in D+/R- LTRs and HTRs

Methods

- Cohort study of High risk (D+/R-) CMV LTRs and HTRs
- Transplants Jan.2010 – July.2012
- CMV prophylaxis given for 6 months
- Surveillance done weekly for 4 weeks, then biweekly for the following 8 weeks post prophylaxis cessation
- Follow up for 1 year post transplant
- Immunosuppression unit scale was utilized for overall estimation of net state of immunosuppression in risk factor assessment

Results

Variables	Frequency
Median recipient age (years) (IQR)	48 (28 - 57)
Male n (%)	22 (47)
Type of transplant n (%)	
Double Lung	35 (74)
Single Lung	3 (6)
Heart / Lung	1 (2)
Heart	8 (17)
Underlying Disease n (%)	
Copd	2 (4)
Cystic Fibrosis-Cepacia positive	1 (2)
Cystic Fibrosis-Cepacia negative	12 (26)
Other	32 (68)
Median duration of prophylaxis (IQR)	182 (115 -198)
Neutropenia n (%)	14 (30)
Leukopenia n (%)	38 (81)
Median duration between cessation of prophylaxis and CMV diagnosis (IQR) N = 36	45.5 (31 - 84.5)
Immunosuppression at CMV diagnosis (n)	**Median (IQR)**
Cyclosporine level (26)	229 (179 - 281)
Tacrolimus level (16)	11.40 (9.2 - 13.7)
Median MMF dose (mg) (29)	1500 (1000 - 2000)
Median azathioprine dose (mg) (4)	87.50 (50 - 100)
Median prednisone dose (mg) (38)	12.5 (10 - 15)

IQR: interquartile range, COPD: chronic obstructive pulmonary diseases, MMF: Mycophenolate mofetil

Table-1: Baseline demographics

Outcome	Total D+/R- LHTR N =47 (%)	Lung Transplant Cohort N = 39 (%)	Heart Transplant Cohort N = 8 (%)
CMV Disease	25 (53)	19 (49)	6 (75)
CMV Infection	17 (36)	16 (41)	1 (13)
Hospitalizations Due to CMV	15 (32)	8 (21)	6 (75)
Compliance to Protocol	16 (34)	16 (41)	0 (0)
Compliance & CMV Disease	7 (44)	7 (44)	0 (0)

Table-2: Outcomes and compliance to protocol

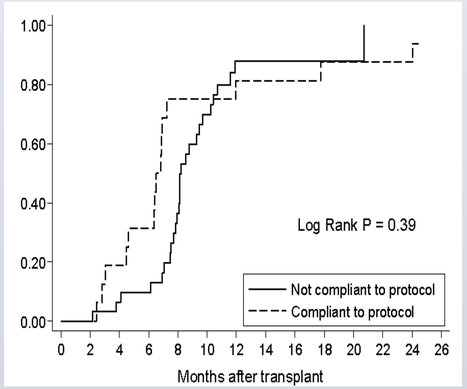

Figure-1: Kaplan Meier curve for cumulative probability of CMV disease

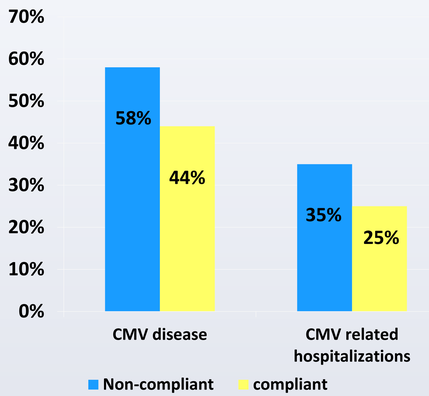

Figure-2: Comparison of outcomes in compliant vs non compliant group

Variables	Number of patients
Median duration between rejection and CMV disease/infection (days) N= 26	127 (42 - 191)
Rejection before CMV infection/disease in LTRs n (%)	19 (54)
Rejection before CMV infection/disease in HTRs N (%)	7 (100)

Table-3: CMV events (infection/disease) and acute rejection episodes

Risk factors	Hazard Ratio	95% C.I.		P value
Acute rejection before CMV diagnosis	**2.18**	**1.11**	**4.28**	**0.02**
Diabetes	**1.59**	**0.86**	**2.95**	**0.14**
Duration of prophylaxis (days)	**0.997**	**0.99**	**1.00**	**0.04**
Age (every one year increase)	**1.03**	**1.01**	**1.06**	**0.003**

Table-4: Risk factors for CMV infection/disease

Conclusions

- Late CMV infection developed in 36% of patients, all were pre-emptively treated and none progressed to CMV disease
- Compliance to post CMV prophylaxis surveillance protocol resulted in a 14% and 10% absolute reduction in late CMV disease and CMV related hospitalizations respectively
- Incidence of late CMV disease remained substantially even with compliance to protocol at 44%
- Longer CMV prophylaxis is associated with lower incidence of CMV disease
- Acute rejection and older age may place D+/R- LTRs and HTRs at risk for CMV disease
- Prophylaxis versus monitoring and pre-emptive CMV treatment during acute rejection episodes should be evaluated in prospective randomized studies