

2648. Terminating the Troll of Transplantation: Letermovir for Cytomegalovirus Prophylaxis

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Background: Letermovir is a novel antiviral that was approved for cytomegalovirus (CMV) prophylaxis after allogeneic hematopoietic stem cell transplant (allo-HSCT). The objective was to assess the real-world outcomes of CMV prophylaxis with letermovir compared with preemptive therapy (PT) alone.

Methods: This retrospective pre- and post-study evaluated the clinical impact of using letermovir prophylaxis in CMV-seropositive allo-HSCT recipients at our institution. The electronic medical record was used to identify patients that received PT alone from July 2016 to November 2017 and letermovir prophylaxis from November 2017 to March 2019. The primary endpoint was the proportion of patients with CMV infection requiring PT through week 24 after transplant. Secondary endpoints included the proportion of patients with CMV infection requiring PT through week 14 after transplant, time to CMV infection requiring PT, incidence of CMV disease, CMV-related hospitalization and all-cause mortality through week 14 and 24 after transplant. Safety data included incidence and time to engraftment and adverse effects due to letermovir. Chi-squared and *t*-test were utilized for categorical and continuous data respectively.

Results: The baseline characteristics were similar (Table 1) and 78.7% of patients were high risk for CMV. Fewer patients in the letermovir group (*n* = 50) than in the historic control group (*n* = 100) had CMV infection requiring PT through week 24 after transplant (9 [18%] vs. 63 [63%], *P* < 0.001). The mean time to CMV infection requiring PT through week 24 after transplant was 93.4 days (28–161) in the letermovir group vs. 37.4 days (11–126) in the historic control group (*P* < 0.001). The all-cause mortality and incidence of CMV-related hospitalization were not statistically different between the two groups through week 24 after transplant (Table 2). The incidence and time to engraftment were not statistically different between the two groups (Table 3).

Conclusion: Letermovir prophylaxis in the real-world setting resulted in less CMV infection requiring PT when compared with a historic control of patients receiving PT alone. The majority of patients in the letermovir group experienced delayed-onset CMV reactivation. Letermovir was well-tolerated with no apparent myelosuppressive toxicities.

Baseline Characteristics	Letermovir Group (n = 50)	Historical Control Group (n = 100)
Age – mean (range), years	56 (21–77)	59 (24–76)
Male sex – n (%)	29 (58)	57 (57)
Prior transplantation – n (%)	4 (8)	13 (13)
Allogeneic – n (%)	2 (50)	11 (85)
Autologous – n (%)	2 (50)	2 (15)
Indication for allo-HSCT – n (%)		
Acute myeloid leukemia	21 (42)	38 (38)
Myelodysplastic syndrome	8 (16)	12 (12)
Non-Hodgkin's lymphoma	5 (10)	8 (8)
Acute lymphoblastic leukemia	7 (14)	15 (15)
Other	9 (18)	27 (27)
Stem cell source – n (%)		
Peripheral blood	35 (70)	75 (75)
Bone marrow	15 (30)	25 (25)
Cord blood	0 (0)	0 (0)
HLA matching donor type – n (%)		
Matched related	9 (18)	23 (23)
Matched unrelated	26 (52)	38 (38)
Mismatched related	13 (26)	38 (38)
Mismatched unrelated	2 (4)	1 (1)
Haploidentical related donor – n (%)	12 (24)	37 (37)
CMV-seropositive donor – n (%)	21 (42)	53 (53)
Myeloablative conditioning regimen – n (%)	41 (82)	81 (81)
Antidysmyocyte globulin use – n (%)	26 (52)	41 (41)
Alemtuzumab use – n (%)	0 (0)	0 (0)
Immunosuppressant regimen – n (%)		
Tacrolimus/methotrexate	35 (70)	64 (64)
Tacrolimus/mycophenolate mofetil/cyclophosphamide	13 (26)	35 (35)
Other	2 (4)	1 (1)
Time to transplant from admission – mean (range), days	8 (4–92)	6 (0–29)
Time to initiation of letermovir – mean (range), days	2 (-6–24)	N/A
CMV >137 IU/mL detected at transplant – n (%)	1 (2)	4 (4)
Risk of CMV disease – n (%)		
High risk	39 (78)	79 (79)
Low risk	11 (22)	21 (21)

Table 2: Primary and Secondary Endpoints

Outcome	Letermovir Group (n = 50)	Historical Control Group (n = 100)	P-Value
Endpoints through week 14 after transplant			
Proportion of patients with CMV infection requiring PT – n (%)	4 (8)	62 (62)	<0.001
Time to CMV infection requiring PT – mean (range), days	38.3 (28–62)	36 (11–80)	0.769
CMV disease (biopsy proven) – n (%)	1 (2)	0 (0)	0.156
CMV related hospitalization – n (%)	0 (0)	2 (4)	0.315
All-cause mortality – n (%)	6 (12)	7 (7)	0.306
Endpoints through week 24 after transplant			
Proportion of patients with CMV infection requiring PT – n (%)	9 (18)	63 (63)	<0.001
Time to CMV infection requiring PT – mean (range), days	93.4 (28–161)	37.4 (11–123)	<0.001
CMV disease (biopsy proven) – n (%)	1 (2)	0 (0)	0.156
CMV related hospitalization – n (%)	0 (0)	2 (4)	0.315
All-cause mortality – n (%)	7 (14)	12 (12)	0.728

Table 3: Safety Endpoints

Outcome	Letermovir Group (n = 50)	Historical Control Group (n = 100)	P-Value
Endpoints through week 24 after transplant			
Incidence of engraftment – n (%)	48 (96)	97 (97)	0.748
Time to engraftment – mean, days	15.4	15.8	0.691
Adverse effects due to letermovir – n (%)			
Gastrointestinal symptoms	8 (16)	N/A	N/A

Disclosures. All authors: No reported disclosures.

2649. Measles-Containing Vaccination Resulted in a Balanced Cytokine Profile Without Evidence of Immunosuppression in Healthy 12-Month-Old Children

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Background: Measles virus infection results in immune activation, viral clearance and lifelong immunity. In addition, there is an immunosuppressive state defined by type 2 skewing of CD4⁺ T-cell cytokine production and induction of regulatory T cells with reduced dendritic cell (DC) activation in the recovery phase. Studies following measles immunization show conflicting immune profiles. To more robustly interrogate and define specific functional cytokine profiles, this study evaluated cytokine profiles in 12-month old infants before and after primary MMR vaccination.

Methods: Cytokine profiles using luminex assay (62-plex; eBioscience) were measured in 65 infants before and 42 days after MMR vaccination administered at 12 months of age as part of a randomized clinical trial. Mean cytokine percentages of children with increased or decreased concentrations of each cytokine in the post sample compared with the levels in the pre sample were evaluated using Student's *t*-test. Cytokines were arranged into dominant CD4⁺ T-cell type, Th1, Th2, and T regulatory (T_{reg}) and those produced by DC.

Results: No dominant cytokine pattern emerged following measles immunization, with a balanced profile. The mean percentage of children with increased and decreased concentrations (pg/mL) of signature CD 4+ T-cell Th1 (tumor necrosis factor alpha [TNFα], interferon gamma [IFNγ]), Th2 (Interleukin [IL] IL5, IL4, IL13), T_{reg} (IL10, transforming growth factor-β TGFβ) and DC (IL12P40 and IL12P70) cytokines were equivalent when measured at 42 days after MMR vaccine compared with levels before vaccine (Table 1) (*P* ≥ 0.05 for all comparisons).

Conclusion: In contrast to data demonstrating an immune suppression profile following measles disease, measles-containing vaccine did not suppress Th1 CD4+ T-cell and DC cytokines or promote Th2 and T_{reg} CD4+ T-cell cytokines measured 42 days after vaccination. The cytokine profile represents one of balance and homeostasis. This study supports the data that show measles vaccine does not cause immunosuppression in healthy infants.

Table 1. Cytokine Profile Following Measles-containing Vaccination in 12-month-old Infants.

Cell Phenotype	Cytokine	Decreased (mean %)*	Increased (mean %)*
Th1 CD4+ T cell	IFNγ	43	57
	TNFα	43	57
Th2 CD4+ T cell	IL5	41	59
	IL4	49	51
Treg CD4+ T cell	IL10	43	57
	TGFβ	49	51
Dendritic Cell	IL12P40	39	61
	IL12P70	41	60

*Mean concentration (pg/ml) of cytokine determined as post-vaccine concentration compared with prevaccine concentration.

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2650. Evaluating Antiviral Agents for Human Noroviruses Using a Human Intestinal Enteroid Model

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