**Policy: CMV Protocol in Liver Transplantation**

**Statement:**
**1. Affected Department:** LiverTransplant Program

**2. Vision Strategy:** Patient Care

**3. Policy Statement:** The Emory Transplant Center will comply with all applicable federal, state and local laws, regulations and policies regarding the management of prescribing medications and refills.

**4. Basis**: This policy is necessary for the protection of patients, physicians and staff

**5. Administrative Responsibility:** Section heads, physicians, practitioners, and staff are responsible for compliance with this policy.

**Scope/Procedure:**

**Protocol:**

**1.** **Cytomegalovirus (CMV) negative liver recipients prior to transplant:** Patients undergoing liver transplantation who are CMV negative will have CMV status rechecked at time of transplantation.

**2.** **All patients** will be **informed** of their donor/recipient CMV status and risk for CMV disease by the post-transplant coordinator during the patient’s transplant admission and documented on the appropriate clinical transplant pathway.

**3**. **Monitoring and Prophylaxis Post Transplant**:

a) Prophylaxis:

High risk (CMV D+/R-) recipients will receive valganciclovir (Valcyte) 900mg PO daily for 3 months. Patients unable to take oral medication will be given ganciclovir 5mg/kg IV daily until able to take oral medication.

Intermediate risk (D+/R+, D-/R+) and low risk (D-/R-) recipients should receive acyclovir for HSV/VZV prophylaxis for 3 months. Alternatively, patients may receive valacyclovir for HSV/VZV prophylaxis (see antiviral protocol)

Medications should be dose reduced for renal insufficiency (see figure 2 below)

b) Monitoring:

For high risk patients, CMV PCR will be monitored weekly starting at month 3 and continuing through month 6, then at 9 and 12 months, and when otherwise clinically indicated.

For intermediate or low risk patients, PCR will be monitored weekly for 3 months after transplant, every other week during months 4 through 6, at 9 and 12 months, and when otherwise clinically indicated.

c) In addition to above monitoring, PCR testing for CMV will be performed whenever a post-liver transplant patient presents with symptoms of fever, low white count, diarrhea, malaise, altered mental status or if CMV viremia is suspected.

**4.** **Treatment of CMV:**

For CMV mismatch (D+/R-) or naïve (D-/R-) patients, if a patient has evidence of CMV replication by PCR (low positive result or higher count), the patient should begin treatment immediately. For experienced and asymptomatic patients (any R+), weekly monitoring without treatment is acceptable. Symptomatic patients (fever, GI symptoms, etc.) should be treated regardless of CMV level in the blood. If monitoring, CMV levels >1000 IU/mL should receive treatment regardless of symptoms.

Treatment should continue until the patient has two “undetectable” CMV PCRs, separated by at least 7 days, if possible.

**Figure 1. Treatment Dosing** **of Antivirals for CMV**

|  |  |  |
| --- | --- | --- |
| Creatinine Clearance (ml/min) | Valganciclovir (mg) – Oral\* | Ganciclovir (mg) - IV |
| ≥60 | 900 mg PO q12 hours | 5 mg/kg IV q 12 hours |
| 40-59 | 450 mg PO q12 hours | 2.5 mg/kg IV q 12 hours |
| 25-39 | 450 mg PO daily | 2.5 mg/kg IV daily |
| 10-24 | 450 mg PO every other day | 1.25 mg/kg IV daily |
| < 10 | 450 mg PO post hemodialysis (3 times/week) | 1.25 mg/kg IV post hemodialysis (3 times/week) |

**\* IV ganciclovir is an alternative for patients unable to tolerate oral medications. If inadequate clinical response, contact the Transplant ID service.**
**Secondary Prophylaxis:**
Secondary prophylaxis may be considered for select patients. For patients that developed CMV viremia/disease while on primary prophylaxis, prophylaxis should be continued after treatment until the end of the previous term or 8 weeks after undetectable CMV PCR, whichever is later. Prophylaxis may be considered after treatment for those patients with recurrent CMV. For patients treated for acute cellular rejection with thymoglobulin, secondary prophylaxis is recommended for three months.

**Figure 2. Antiviral Dosing for Prophylaxis or Maintenance Dosing of Antivirals for CMV**

|  |  |  |
| --- | --- | --- |
| Creatinine Clearance (ml/min) | Valganciclovir (mg) – Oral | Ganciclovir (mg) - IV |
| > 60 | 900 mg PO daily | 5 mg/kg IV q24 hours |
| 40-59 | 450 mg PO daily | 2.5 mg/kg IV q24 hours |
| 25-39 | 450 mg PO every other day | 2.5 mg/kg IV q24 hours |
| 10-24 | 450 mg PO 3 times/week | 1.25 mg/kg IV q24 hours |
| < 10 | 450 mg PO post hemodialysis or 2-3 times/week | 0.625 mg/kg IV post hemodialysis (3 times/week) |

**\* IV ganciclovir is an alternative for patients unable to tolerate oral medications.**
**5**. **Surveillance during and Post Treatment**:

a) Patients should have a CMV PCR checked weekly while on treatment.

b) Once treatment ends PCR surveillance will continue every other week for 6 weeks.

c) Patients on secondary prophylaxis do not require PCR monitoring while receiving prophylaxis.

**6.** **Transplant ID Referral:**
All patients treated for **CMV disease** (not viremia) should be referred for follow up in the Transplant ID Clinic to be seen within 2-3 weeks of initiating therapy. Patients with CMV viremia should be seen by Transplant ID if there is a lack of response to therapy or have significant myelosuppression from CMV or CMV treatment.

**7.** **Monitoring, Prophylaxis and Treatment of the Liver-Kidney Transplant Recipients:**
For post-transplant liver-kidney recipients, monitoring, prophylaxis and treatment of CMV should default to the Emory Transplant Center Liver Transplant CMV Protocol (see ETC Policy and Procedures: Kidney (and Pancreas) CMV Protocol.

**8. Policy Review:**
As part of the QAPI program, policy compliance and CMV viremia rates for the first twelve months post-transplant will be reviewed by the transplant program’s clinical leadership and transplant infectious disease specialists.

**References:**
Kotton CN, Kumar D, Caliendo AM, et al. Updated International Consensus Guidelines on the Management of Cytomegalovirus in Solid-Organ Transplantation. Transplantation 2013;96,

Razonable, RR. Cytomegalovirus Infection after Liver Transplantation. Liver Transplantation 2010;16: s45-s53.

Taber DJ, Ashcraft E, Baillie GM, et al. Valganciclovir prophylaxis for patients at high risk developing cytomegalovirus disease. Transpl Infect Disease 2004;6: 101-109.

Kalil AC, Levitsky J, Lyden E, et. al. Meta-Anaylsis: The efficacy of strategies to prevent organ disease by cytomegalovirus in solid organ transplant recipients. Ann Int Med 2005; 143: 870-880.

Fishman JA. Infection in solid-organ transplant recipients. NEJM 2007; 357: 2601-2614.

**Related Policies/Procedures: Concomitant medications, Anti-Viral Protocol in Liver Transplantation**

Approved by: Liver Transplant Leadership Group