**Policy: Post-Liver Transplant Renal Sparing Protocol**

**Statement:**
**Affected department**: Liver transplant program
**Vision strategy**: Patient care
**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.
**Basis**: This policy is necessary for the protection of patients, physicians and staff.
**Administrative Responsibility**: Section heads, physicians, practitioners, and staff are responsible for compliance with this policy.

**Scope/Procedure:**

Medications used in patients with calcineurin inhibitor (CNI) induced renal dysfunction

**I. Diagnosis of calcineurin inhibitor (CNI) induced renal dysfunction**

a. A serum creatinine that fails to improve or continues to rise despite CNI minimization or CNI elimination. CNI induced renal dysfunction may be presumed in cases that other causes of renal insufficiency are ruled out.

b. To quantify GFR, obtain twenty-four hour urine collection with urine creatinine to protein ratio and evaluate presence of proteinuria.

i. Patients with proteinuria < 800mg and GFR > 40ml/min, the patient may be a candidate for conversion to sirolimus.
ii. Patients with significant proteinuria (>800mg) or reduction in GFR (<40ml/min) may have worsening renal function if converted from a CNI to sirolimus.

**II. Mycophenolate mofetil (CellCept)**

Mycophenolate mofetil has been useful in limiting calcineurin dosing to help maintain or improve renal function. Patients that meet the diagnosis above should be started on CellCept (mycophenolate mofetil) 1000mg PO q12hr if not currently receiving.

**III. Prednisone**

Prednisone may be useful in limiting calcineurin dosing to help maintain renal function. Consider adding prednisone to the immunosuppression regimen if not currently receiving.

**IV. Sirolimus (Rapamune**)

Conversion from a CNI to sirolimus may help maintain or improve renal function. Sirolimus conversion should be considered if a patient has a creatinine clearance consistently below 60 mL/min or increased SCr from baseline. Sirolimus may also have beneficial anti-tumor effects as well and may have a role in patients with skin cancer, HCC, renal cell carcinoma or other malignancies.

b. Patients should be > 30 days post liver transplant before considering conversion to sirolimus. Staples should be removed and the wound should be healed.

c. Prior to the initiation of sirolimus, patients should have the following lab values obtained: baseline fasting lipid profile (FLP) including triglycerides, baseline fasting glucose, HbgA1c, and a spot urine for protein. If protein is >800mg, the patient may not benefit from sirolimus conversion.

d. To convert patients to sirolimus, on the day of conversion, the CNI inhibitor dose should be decreased by 50%. Sirolimus should be started at 2-3 mg daily. Sirolimus trough level should be obtained 5-7 days after initiation of therapy. Goal sirolimus trough level is 5-12 ng/ml, depending on the time from transplant/patient situation. Dosage should be increased by 1 mg increments if not within therapeutic range. Once a therapeutic level is achieved, then the CNI should be discontinued. Sirolimus trough levels should be obtained weekly until therapeutic, then may be obtained q 2 weeks or longer frequency once stable. Patients started on sirolimus should also be receiving mycophenolate mofetil and/or prednisone as monotherapy may increase the risk for acute cellular rejection (ACR). For most patients, sirolimus should not be used as monotherapy.

e. Potential side effects of sirolimus include, but are not limited to: Hepatic artery thrombosis (HAT), delayed wound healing, mouth ulcers, edema, pancytopenia, hypertriglyceridemia, pneumonitis.

**V. Laboratory monitoring for sirolimus conversion**

a. To monitor CNI conversion, the following labs should be monitored:

Serum creatinine, BUN, tacrolimus or cyclosporine levels, sirolimus levels, LFTs, signs/symptoms of rejection, CBC, cholesterol and signs/symptoms infection. Labs should be obtained no less than q 2 weeks during the conversion.
ii. A fasting lipid profile should be obtained in 1-3 months after initiation of sirolimus therapy.

**VI. Everolimus (Zortress)**

a. Conversion from a CNI to everolimus may help maintain or improve renal function. Everolimus conversion should be considered if a patient has a creatinine clearance consistently below 60 mL/min or increased SCr from baseline. Everolimus may also have beneficial anti-tumor effects as well and may have a role in patients with skin cancer, HCC, renal cell carcinoma or other malignancies.

b. Patients should be > 30 days post liver transplant before considering conversion to everolimus. Staples should be removed and the wound should be healed.

c. Prior to the initiation of everolimus, patients should have the following lab values obtained: baseline fasting lipid profile (FLP) including triglycerides, baseline fasting glucose, HgA1C, and a spot urine for protein. If protein is >800mg, the patient may not benefit from everolimus conversion.

d. To convert patients to everolimus, on the day of conversion, the CNI inhibitor dose should be decreased by 50%. Usual starting dose of everolimus is 1-1.5mg po q12hr. Everolimus trough level should be obtained 5 days after initiation of therapy. Goal everolimus trough level is 3-12 ng/ml, depending on the time from transplant/patient situation. Dosage should be increased by 0.5 to 1 mg increments if not within therapeutic range. Everolimus trough levels should be obtained weekly until therapeutic, then may be obtained q 2 weeks or longer frequency once stable. Patients started on everolimus should also be receiving reduced dose CNI, mycophenolate mofetil and/or prednisone as monotherapy may increase the risk for ACR. Currently the Emory University Lab runs and reports everolimus levels daily.

e. Potential side effects of everolimus include, but are not limited to: Proteinuria, hypertriglyceridemia, pancytopenia, delayed wound healing, edema, mouth ulcers, new onset diabetes, male infertility, pneumonitis

**VII. Laboratory monitoring for everolimus conversion**

a. To monitor CNI conversion, the following labs should be monitored

i. Serum creatinine, BUN, tacrolimus or cyclosporine trough levels, everolimus trough levels, LFTs, signs/symptoms of rejection, CBC, blood sugars, proteinuria, cholesterol and signs/symptoms infection. Labs should be obtained no less than q 2 weeks during the conversion.
ii. A fasting lipid profile should be obtained in 1-3 months after initiation of everolimus therapy.

b. Conversion to a CNI should be considered in any patient on everolimus undergoing a surgical operation, such as a hernia repair, prior to the scheduled surgical date to help promote better would healing post procedure. Patients may be converted back to everolimus after the wound is healed.

References**:**
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Approved by: Liver Transplant Leadership Group

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