The Transplant Institute METHODIST DALLAS **Methodist Dallas Medical Center**	**Title:** Immunosuppression Protocol **Section:** Liver	**Effective Date:** 04/06/2004
Approved by: Alejandro Mejia, M.D., Surgical Director of Liver Transplant Program Jeffrey Weinstein, MD, Medical Director of Liver Transplant Program Melody Holder, Director of Transplant Clinical Operations		Revision Date(s): 05/13/2004; 04/07/2009; 09/20/2010; 02/03/2015; 03/23/2017; 06/23/2020; 06/29/2021; 10/2024 Next review Date: 10/2027

Purpose: To ensure uniform management of immunosuppression post liver transplantation

Procedure:

1) **Primary Adult Liver Transplantation**

Pre-Op

- Mycophenolate mofetil 1000 mg PO

Anhepatic:

- Solumedrol 500 mg IV

Post-Op

- Mycophenolate mofetil 1000 gm PO BID (Adjust for WBC and GI side effects)
- Tacrolimus 0.1mg/kg divided into two doses (Adjust for blood trough level of 10-12 ng/ml)

  Or:
- Cyclosporine modified 4 mg/kg divided into two doses (Adjust for blood trough level of 200-300 ng/ml)
- Solumedrol 500 mg IV on arrival to SICU
- Solumedrol 250 mg IV on POD 1
- Solumedrol 125 mg IV on POD 2
- Solumedrol 75 mg IV on POD 3
- Solumedrol 50 mg IV on POD 4
- Prednisone 20 mg PO daily beginning on POD 5, then taper as outlined below

  *For patients with a donor-recipient age discrepancy >30 years, consider omitting Mycophenolate mofetil

Steroid Tapering Schedule

- Prednisone 20 mg PO daily through POD 13
- Prednisone 15 mg PO daily through POD 14-27
- Prednisone 10 mg PO daily POD 28-35
- Prednisone 5 mg PO daily POD 36-180
- Taper as indicated on a case-by-case basis considering liver enzymes, pre-operative diagnosis and post-operative course

2) **Re-transplantation**

Pre-Op
Stop tacrolimus/cyclosporine/sirolimus

- Mycophenolate mofetil 1000 mg PO

Anhepatic

- Solumedrol 500 mg IV

Post-Op

- Follow protocol as written for Primary Adult Liver Transplantation but consider a prolonged steroid taper at physician direction

3) **Patients with renal dysfunction** (CVVHD/HD for OLTx, SCr>1.5)

Pre-Op

- Mycophenolate mofetil 1000 mg PO
- Consider induction with Basiliximab 20 mg POD 0 (anhepatic) and 20 mg POD 4

Anhepatic:

- Solumedrol 500mg IV

Post-Op

- Mycophenolate mofetil 1000 mg PO
- Steroids as written for Primary Adult Liver Transplantation
- Delay Tacrolimus administration until oliguria resolves or decreasing SCr in the absence of oliguria
- Then begin Tacrolimus at 1 mg PO BID (Adjust for blood trough level of 5-8 ng/ml)
- Consider Anti-thymocyte globulin if significant renal dysfunction persists at POD 3 and the patient did not receive Basiliximab
- Consider converting to an mTOR inhibitor id renal dysfunction persists greater than one month

4) **Treatment of Acute Rejection**

A liver biopsy is recommended in 24-48 hours for all cases of suspected rejection. However, specific patient situations may preclude obtaining a biopsy. In these circumstances there should be documentation in the medical record as to why a biopsy was not performed. A review with Pathologist is highly recommended.
Post treatment, a repeat liver biopsy is recommended 7-14 days after treatment with IV steroids

Recommendations
RAI 3-4: Consider adjustment in immunosuppression medications only (increase Tacrolimus/Cyclosporine/Mycophenolate mofetil)
RAI 5 or greater: Steroid recycle

Steroid Recycle

- Solumedrol 1000 mg IV day 1
- Solumedrol 1000 mg IV day 2
- Solumedrol 1000 mg IV day 3
- Begin and taper prednisone per "Post-Rejection Treatment Steroid Taper" (below)

If severe rejection is noted on biopsy or if no response to IV steroids by day 3, consider treatment with Anti-thymocyte globulin

- Stop Mycophenolate mofetil while receiving Anti-thymocyte globulin
- Optimize dose of immunosuppression drug

Post-Rejection Treatment Steroid Taper

- Prednisone 40mg PO daily x 7 days then:
- Prednisone 20 mg PO daily x 14 days then:
- Prednisone 15 mg PO daily x 14 days then:
- Prednisone 10 mg PO daily x 7 days then
- Prednisone 5 mg PO daily x 6 months

*Following resolution of acute rejection, maintain a higher trough level of the immunosuppression drug

5) **Patients with Renal Dysfunction – One Month Post OLTx**

In patients with eGFR 45-75 ml/min, may consider Tacrolimus/Everolimus maintenance one month post OLTx

Guidelines

- Urinalysis and fasting lipid panel should be drawn prior initiation of therapy and every 3 months while on Everolimus
- Tacrolimus goal 2-3 ng/ml, Everolimus goal 3-8 ng/ml for a combined goal level of ≤ 8 ng/ml
- Steroids as written for Primary Adult Liver Transplantation
- Mycophenolate mofetil should be discontinued upon Everolimus initiation
- Everolimus is not to be used in patients with hernia, wound infections or pending surgeries

6) **Discontinuing Antifungal (Diflucan)**

- Consult provider for dose adjustment in Tacrolimus and Cyclosporine
- Repeat trough level at 48 hours and 7 days after discontinuation

7) **Continuing Sirolimus**

High Risk HCC, worsening renal function or adverse effects of CNI

Guidelines

- Everolimus should be used for new prescriptions or if Sirolimus is denied
- Check urinalysis and lipids months 1, 4, 12 and annually
- Contraindications include open wounds, hernias and biliary complications