UCMC Liver Transplant Program – Treatment of Biopsy Proven Cellular Rejection

Mild Rejection

1) Consult Transplant Hepatology

2) Adjust maintenance immunosuppressive regimen (physician discretion); options include:
   a) Increase tacrolimus dose to achieve higher trough
      -Aim for trough 4 points above current maintenance trough target
      - Consider Scr level
   b) Initiate/Increase mycophenolate mofetil (MMF)
      -Dose up to a maximum of 1g twice daily as tolerated
      -Consider WBC level
   c) Initiate steroids 20mg daily or increase current steroid dose

3) Reassess liver tests in 2-3 days

4) Upon resolution evaluate reason(s) for rejection and adjust maintenance regimen as necessary to prevent recurrence

Indeterminate Rejection

1) Consult Transplant Hepatology

2) If physician review of biopsy slides is considered to be consistent with rejection refer to corresponding treatment

Moderate to Severe Rejection

1) Consult Transplant Hepatology
2) Treatment based on rejection TYPE (acute/chronic; cellular/antibody) and SEVERITY (mild/moderate/severe)
3) **OUTPATIENT (moderate rejection) → Administer Prednisone PO Therapy**
   a) Day #1-3 = Prednisone 60mg po daily. Evaluate need for blood sugar monitoring (order necessary supplies if needed)
   b) Day #4 = reassess liver tests
      IF improved: continue therapy and monitoring of liver tests; consult Tx Hep to determine taper[1]
      IF NO improvement or worsening: admit for methylprednisolone (MP) IV therapy
4) **INPATIENT (moderate/severe rejection) → Methylprednisolone (MP) IV Therapy x 3 doses** (and optimize maintenance)
   A) Days #1-3 = MP 500mg IV x 1 dose (DAY 1)
      MP 250mg IV x 1 dose (DAY 2)
      MP 250mg IV x 1 dose (DAY 3)
      Evaluate need for stomach acid suppressive therapies
   B) Day #4 = reassess liver tests
      1) IMPROVED: MP 125mg IV x 1 dose; then steroid taper[1]
      2) NOT IMPROVED or WORSE: Repeat biopsy, consider AMR (i.e. obtain DSA and C4d staining)
         a) Biopsy improved: MP 125mg IV x 1 dose; then steroid taper[1]
         b) Biopsy not improved: Thymoglobulin 1.5mg/kg/dose to achieve 7 days of absolute CD3 suppression (goal CD3 < 25
            - Dose Thymo daily as needed to achieve 7 days of absolute CD3 suppression < 25
            - Round Thymo dose to nearest 25mg. Cumulative max Thymo dose of 6 mg/kg
            - Premedicate 30-60 minutes prior to Thymo administration with:
              (1) Acetaminophen 650mg po, (2) Diphenhydramine 25mg IV/po and (3) MP 60mg IV
            - Additional Thymo doses and/or extending therapy length may be necessary depending on clinical situation (physician discretion)
            - Recycle Anti-infective Prophylaxis for certain patient populations receiving Thymo per table

	Patient Population	Medication / Dose[2]	Duration
PCP	All	Bactrim SS 1 tab po daily	6 months
CMV	HIGH Risk (D +/ R -)	Valcyte 900 mg po daily	6 months
	INTERMEDIATE Risk (D+/R+;D-/R+)	Valcyte 450 mg po daily	3 months

[1]STEROID TAPER
- Individualize based on patient situation (i.e. shortened for acute episodes due to subtherapeutic CNI levels; extended for chronic episodes)
- Adjust based on patient response

C) OTHER THERAPIES may be necessary if antibody mediated rejection and/or ongoing chronic rejection present
D) UPON RESOLUTION: evaluate rejection reason(s); maintenance ISP regimen may require adjustment
E) HOSPITAL DISCHARGE post initiation of rejection treatment
   1) Schedule Tx Clinic visit within 7-14 days
   2) Provide 30 day prednisone prescription (ensure sufficient quantity for taper)
   3) Evaluate need for home blood sugar monitoring (provide order for necessary supplies if needed)
   3) Provide lab order for follow up labs (ensure ordered so that results obtained prior to clinic visit)

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