Antibody Mediated Rejection Treatment Protocol

1. **Baseline Testing**
   - Renal function, kidney biopsy
   - Donor specific antibody (DSA) testing
   - CD19 and C20 subsets

2. **AMR Treatment Protocol (Day 1-15, Day 1 = treatment start date)**
   I. **Steroids:**
      - Pulse methylprednisolone 500 mg IV daily \(\times\) 3 on Day 1,2,3 then prednisone taper as per standard protocol
      - Example: Prednisone 100 mg \(\times\) 1 → 75 mg \(\times\) 1 → 60 mg \(\times\) 1 → 50 mg \(\times\) 1 → 40 mg \(\times\) 1 → 30 mg \(\times\) 1 → 20 mg OD for 4 weeks then slow taper to 5 mg OD

   II. **PLEX and IVIG**: 1-3:
      - PLEX + IVIG daily \(\times\) 3 on Day 1,2,3 then 3 treatments per week for a minimum of 8 sessions. Additional treatments may be indicated based on clinical indication
      - PLEX: 1.5x volume exchange for 3 treatments, then 1x volume exchanges thereafter. When performing PLEX within 48 hours of kidney biopsy replace with FFP, otherwise replacement with 5% albumin
      - IVIG infusion: dosed 100 mg/kg/dose IV given after each PLEX
      - Pre-medicate IVIG infusion with diphenhydramine 25-50 mg IV and acetaminophen 650 mg PO prior to IVIG

   III. **Rituximab (1-2 doses)**:
      - Rituximab 375 mg/m\(^2\)/dose IV given on Day 4 (could be given after PLEX and IVIG if there is adequate time and space)
      - Pre-mediate Rituximab infusion with:
        - Diphenhydramine 50 mg PO/IV prior to Rituximab and Q4hr thereafter
        - Acetaminophen 650 mg PO 30 min prior to Rituximab and Q4hr thereafter
      - Wait for a minimum of 24 hrs (ideally 48 hrs) before resuming PLEX after dosing Rituximab
      - Repeat CD19 and CD20 counts after last plex – if CD19/20 \(\geq\) 5 cells/mm\(^2\), consider giving a second dose of Rituximab

   IV. **Optimization of maintenance immunosuppression**:
      - Increase MMF or Myfortic to full dose (MMF 1g BID and Myfortic 720 mg BID)
      - Up-shift CNI target one level up

   V. **Follow-up and Surveillance**:
      - Consider repeat kidney biopsy before 1-month post treatment based on clinical indication (i.e. inadequate treatment response, worsening renal function, re-assess mixed TCR and AMR); if patient has good clinical response, consider biopsy at 1 month or later
      - Repeat DSA testing at Day 15 (after finishing 8 PLEX sessions), Day 28
Supplement 1: Diagnosis of AMR

- Refer to Banff 2013 Criteria for AMR diagnosis
- A simplified schematic is provided in Table 1

*Note: C4d positivity is no longer required for AMR diagnosis as long as a significant degree of microvascular injury is present (g+ptc ≥ 2)

*AMR treatment may be initiated if clinical and histologic evidence for AMR is strong and DSA and/or non-HLA antibody testing result is pending

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<thead>
<tr>
<th></th>
<th>Acute/Active AMR</th>
<th>Chronic/Active AMR</th>
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<tbody>
<tr>
<td><strong>Histology:</strong></td>
<td>1. Microvascular injury: (g or ptc)</td>
<td>1. Transplant glomerulopathy (cg)</td>
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<td></td>
<td>2. Arteritis</td>
<td>2. Peritubular basement membrane duplication</td>
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<td></td>
<td>3. Thrombotic microangiopathy</td>
<td>3. Arterial intimal fibrosis</td>
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<td>4. ATN-unknown cause</td>
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<tr>
<td><strong>Serology:</strong></td>
<td>Donor-specific antibodies (HLA, AT1R-Ab, MICA)</td>
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<tr>
<td><strong>Interaction:</strong></td>
<td>C4d</td>
<td>Moderate microvascular inflammation (g+ptc &gt;= 2)</td>
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<td>Endothelial cell gene transcripts</td>
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</tbody>
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Table 1. Simplified criteria for diagnosis of AMR, based on Banff 2013 classification.5
References