| The Transplant Institute<br>METHODIST DALLAS<br>Methodist Dallas Medical Center | **Title:**<br>Rejection Treatment | **Effective Date:**<br>02/2012 |
|---|---|---|
| | **Section:**<br>Kidney and Pancreas | |
| **Approved by:**<br>Richard Dickerman, M.D., Surgical Director<br>Jose Castillo-Lugo, M.D., Medical Director<br>Melody Holder, Director of Transplant Clinical Operations | | **Revision Date(s):**<br>07/2016; 06/2021;<br>04/01/2025<br>**Next review Date:**<br>04/2028 |

**Purpose:** To define standard treatment of kidney rejection. Final treatment decision will be made by nephrologist and/or transplant team.

**Policy:** All patients with suspected rejection are to have a renal transplant or pancreatic transplant core biopsy including a C4d stain, as soon as feasible after initiation of anti-rejection therapy.

**Renal Transplant Rejection**

**Acute Cellular Rejection (ACR)**

| Banff Grade 2003 | Rx |
|---|---|
| Type Ia, b | Methylprednisolone 500 mg IV Daily x 5 days |
| Type IIa, b, & Type III | rATG IV Daily x 5-7 days |

1) rATG Dose Adjustment:
   a. 1.5 mg/kg if WBC>3,000 and platelet count >80,000
   b. 0.75 mg/kg if WBC 2,000–3,000 and platelets 50,000–80,000
   c. Hold if WBC <2,000 or platelet count <50,000

   *Note in patients on rATG: If WBC <3,000, Neupogen 300 mcg SubQ may be used to prevent delay in ATG administration

2) Additional Treatment:

   a. Plasmapheresis (1 plasma volume [PV] based on ideal body weight) daily x 5 treatments then QOD x 5 treatments
      - PV=(0.065 x kg) x (1-HCT)

   b. Immunoglobulin (IVIg)100 mg/kg over 2 hours post-pheresis treatment

   c. Adjunctive Therapy:

      - Anti-thymocyte Globulin (Rabbit) [rATG]
      - Bortezomib – 1.4 mg/m² on days 1,4,8,11
      - Eculizumab

Therapy should be individualized for the addition of plasmapheresis according to the antibody titers and how fast serum creatinine is rising. High titers are more likely to be resistant to IVIg alone.

1) Follow monthly DSA, CMV-PCR, BK-PCR
   a. DSA target ≤1:8 dilution
2) If DSA ≥1:16 dilution, repeat IVIG q6 weeks x 4 (maximum dose)
3) Re-biopsy the patient after 6 months if DSA ≥1:16 for assessment of chronic humoral rejection

**Chronic Humoral Rejection**

1) Optimize maintenance immunosuppression
2) IVIg 2 g/kg divided in 4 doses
3) Rituximab 375 mg/m$^2$
4) Solumedrol 100 mg as a premedication to Rituximab and IVIg

**Pancreas Rejection**

a) Diagnosis

| Histologic Classification System<br>Acute Pancreas Allograft Rejection | | |
|---|---|---|
| **Grade** | **Severity** | **Histologic Description** |
| Grade 0 | Normal | Normal pancreas histology |
| Grade 1 | Borderline | Changes consisting of rare lymphocytic septal infiltrates while the acinar parenchyma is free of inflammation |
| Grade 2 | Mild | Mixed inflammatory septal infiltrates with multifocal involvement of acinar parenchyma. Ductal inflammation and/or venulitis are often seen. |
| Grade 3 | Moderate | Septal inflammation with multifocal involvement of acinar parenchyma associated with single cell injury, such as vacuolization, necrosis, or apoptosis. |
| Grade 4 | Moderate with Vascular Rejection | Moderate rejection with arterial endothelitis or vasculitis. |
| Grade 5 | Severe | Extensive inflammatory infiltrates with confluent acinar necrosis. |

b)
c)

b) Treatment Guidelines

1) Grade 0-1 Consider optimizing immunosuppression
2) Grade 2-3 Solumedrol 500 mg IV daily x 5 days
3) Grade 4-5 rATG IV daily x 5-7 days

rATG Dose Adjustment:

a) 1.5 mg/kg if WBC>3,000 and platelet count >80,000
b) 0.75 mg/kg if WBC 2,000–3,000 and platelets 50,000–80,000
c) Hold if WBC <2,000 or platelet count <50,000

*Note in patients on rATG: If WBC <3,000, Neupogen 300 mcg SubQ may be used to prevent delay in ATG administration