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Novel Desensitization and Treatment Strategies for Antibody-Mediated Rejection

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Antibody-mediated rejection (ABMR) remains a leading cause of graft failure in kidney transplantation, representing a significant challenge to long-term allograft survival despite advancements in immunosuppressive therapy. Current therapeutic interventions, including plasmapheresis, intravenous immunoglobulin, and anti-CD20 therapies, have shown limited efficacy in both active and chronic ABMR, underscoring the need for novel, targeted treatment strategies. This presentation explores emerging desensitization and treatment approaches designed to intervene at key points in the immune response. These include: (1) Targeting B cell activation and germinal center responses to prevent the formation and persistence of donor-specific antibodies (DSAs); (2) Targeting plasma cells, the primary producers of DSAs, to suppress ongoing alloantibody production; (3) Targeting alloantibody effector function through strategies that neutralize or eliminate circulating DSAs and inhibit complement activation; (4) Modulating T cell co-stimulation to reduce the support provided to B cell maturation; and (5) Immunomodulatory approaches aimed at reducing inflammation and preventing downstream tissue damage. We will review the mechanisms of these novel therapies and discuss recent clinical trial data demonstrating their efficacy in ABMR management. As precision medicine continues to advance, a multi-targeted approach that integrating B cell depletion, plasma cell inhibition, complement blockade, and inflammation control may offer the most effective strategy to mitigate ABMR and preserve graft function in kidney transplant recipients. The novel therapies targeting the humoral alloimmune response, as discussed in this lecture, will help develop future strategies to prevent and treat ABMR.

Keywords: Antibody-Mediated Rejection, Desensitization, Humoral Alloimmune Response, Kidney Transplantation, Novel treatment strategies