

Table 1. Atypical, Dual Antibody and Drug-Induced Variants of Anti-GBM Disease

Atypical anti-GBM disease ^{30,56}	<p>~5-10% of all Cases of anti-GBM disease have absent circulating anti-GBM antibodies</p> <p>Mild clinical and/or histopathological presentation</p> <p>Management:</p> <p>§ Exclude cases of IgG4-, IgA-, and IgM-mediated anti-GBM disease using modified assays</p> <p>§ Thorough evaluation for atypical IgG antibodies using highly sensitive assays and modified assays targeting newer epitopes/antigens</p>
Dual anti-GBM antibody and anti-MPO antibody positive disease ^{21,22,37,53}	<p>~20-40% of all cases of anti-GBM disease</p> <p>Older age and more systemic manifestations than classic anti-GBM disease</p> <p>Relapse commoner than classic disease</p> <p>Outcomes similar to classic disease</p> <p>Management:</p> <p>§ Initial phase is similar to classic anti-GBM disease;</p> <p>§ Maintenance immunosuppression to prevent relapse akin to AAV</p>
Drug-induced anti-GBM disease ⁵⁷⁻⁶⁸	<ol style="list-style-type: none"> 1. Anti-CD52 monoclonal antibody (alemtuzumab) is associated with the classic anti-GBM disease after 9-10 months of administration in genetically susceptible patients 2. TNF-alpha antagonists (etanercept, adalimumab) are associated with classic anti-GBM disease. The exact pathogenesis is unclear as TNF-alpha blockers are known to prevent/resolve anti-GBM GN in animal models. 3. Immune checkpoint inhibitors: Anti-programmed death-1 (nivolumab, pembrolizumab), CTLA4 antagonist (tremelimumab), kinase inhibitors (dabrafenib, trametinib) are associated with classic and atypical forms of anti-GBM disease 4. SARS-CoV-2 vaccines: Among all other de novo primary GNs reported, anti-GBM disease is rare after this vaccine. All types of SARS-CoV-2 vaccines such as mRNA, Pfizer-BioNtech, and AstraZeneca are associated with classic anti-GBM disease <p>Management: Drug withdrawal + treatment similar to classic anti-GBM disease</p>

Abbreviations: GBM, glomerular basement membrane; GN, glomerulonephritis; Ig, immunoglobulin; MPO, myeloperoxidase; TNF, tumor necrosis factor.

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