B-Cell Therapy & Podocytopathies

Adrian Liew
Singapore

DISCLOSURES

Consultant/Advisory Boards/Steering Committees:

ADARx Pharmaceuticals, Alexion Pharmaceuticals, Alnylam Pharmaceuticals, Alpine Immune Sciences, Arrowhead Pharmaceuticals, AstraZeneca, Baxter Healthcare, Bayer AG, BioCryst Pharmaceuticals, Biogen, Boehringer-Ingelheim, Chinook Therapeutics, Dimerix Limited, Eledon Pharmaceuticals, George Clinical, GlaxoSmithKline, Kira Pharmaceuticals, Novartis, Prokidney, Otsuka Pharmaceuticals, Takeda Pharmaceuticals, Timberlyne Therapeutics, Vera Therapeutics, Vertex Therapeutics, Visterra Inc, Zai Lab Co. Ltd

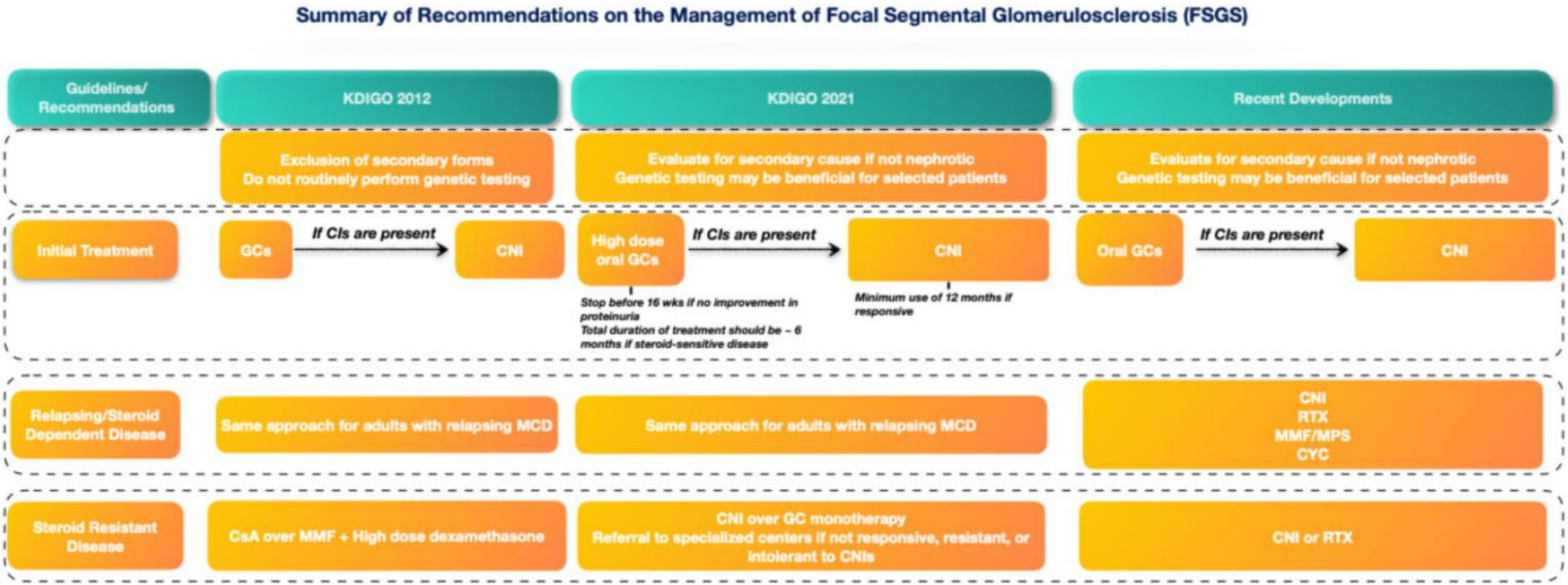
Speakers' Bureau:

AstraZeneca, Baxter Healthcare, Boehringer-Ingelheim, Chinook Therapeutics, Everest Medicines, Otsuka Pharmaceuticals, Vera Therapeutics, Vertex Therapeutics

Data Safety and Monitoring Committees

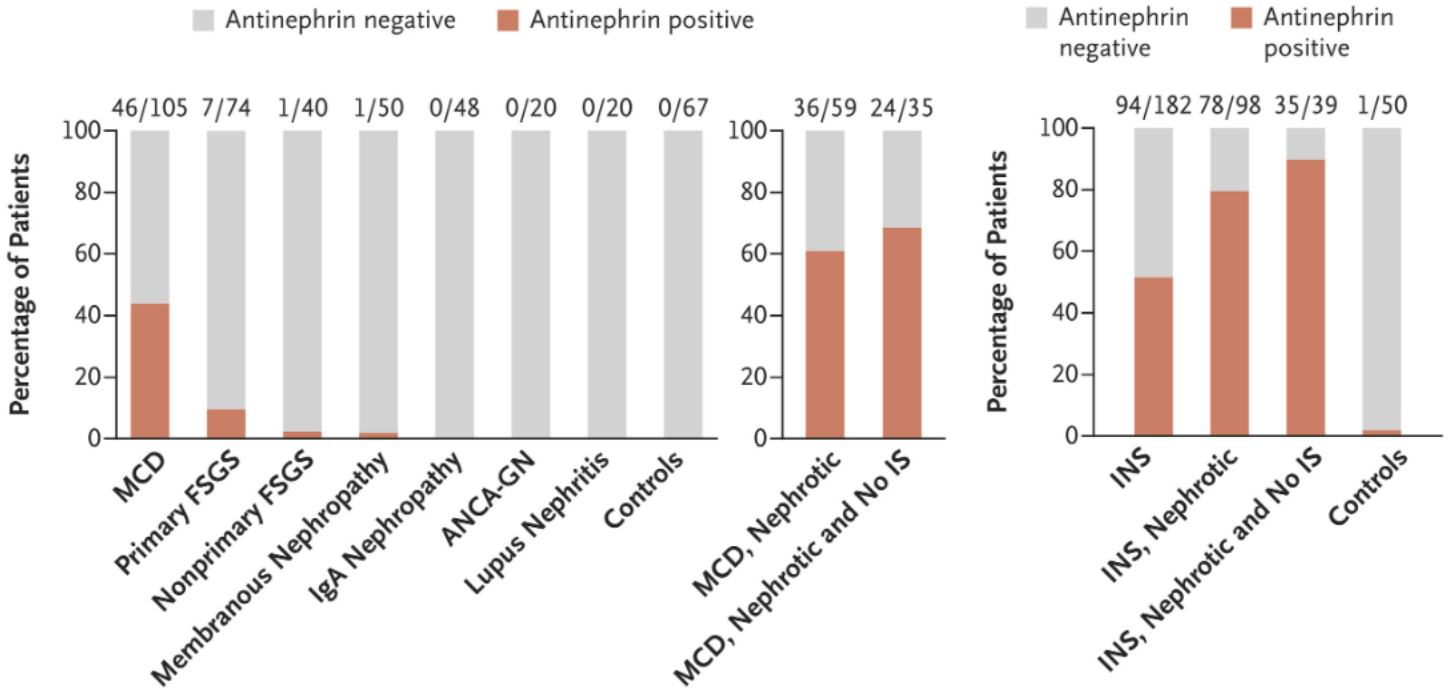
Dimerix Limited and Zai Lab Co. Ltd.

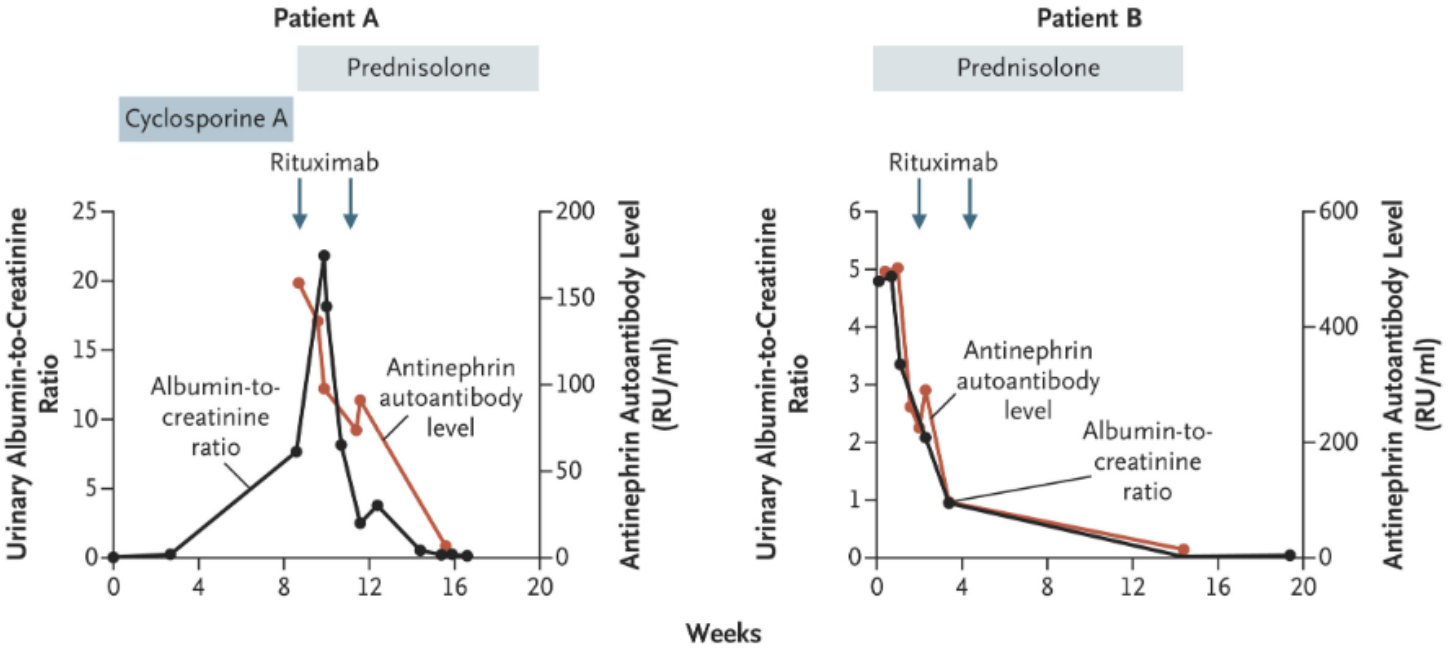
Treatment Landscape for Podocytopathies

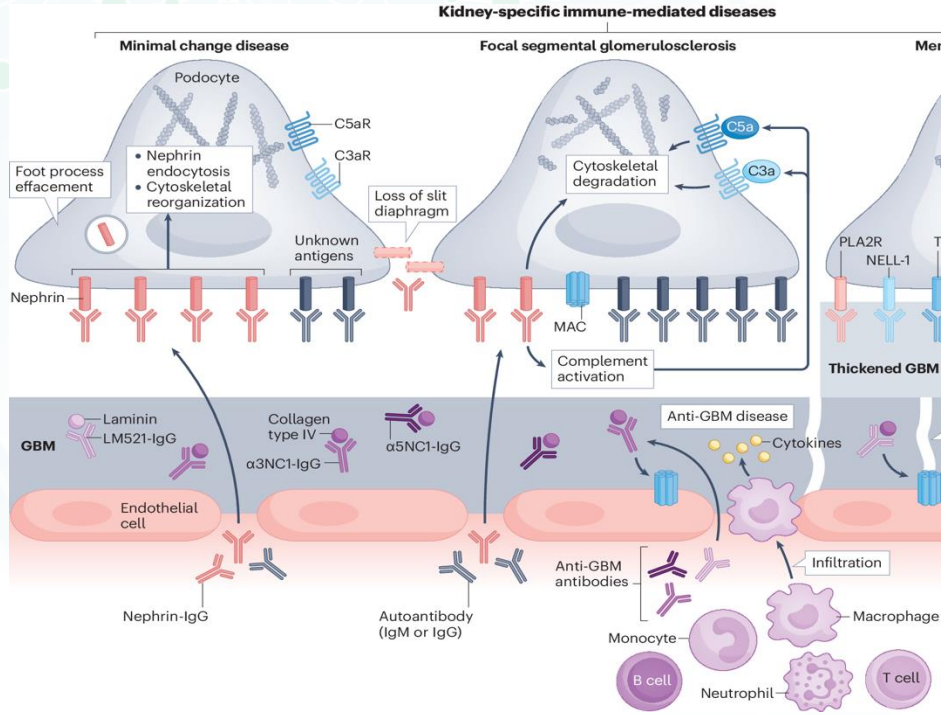


Mirioglu S et al. Nephrol Dial Transplant 2024; 39:569-580.

Autoantibodies in Podocytopathies







Hengel FE et al. N Eng J Med 2024; 391:422-433.
Cui Z et al. Nat Rev Nephrol 2024; 20:639-640.

Rituximab vs Obinutuzumab vs Anti-CD38 in Podocytopathies

Rituximab	
Emerging data for frequently relapsing/steroid dependent MCD: - *Median time to relapse is longer* - *Complete remission rates as high as 87.3% in a meta-analysis* - *Maintenance of remission with repeated doses*	**Ongoing/Planned Studies:** • **Phase 2 MCD (Incidence of Relapse at M12: NCT 03970577)** • **Phase 2/3 MCD (Incidence of relapse within 12 months: NCT05786768)** • **Phase 2/3 MCD/FSGS (with Daratumumab, relapse within 12 months: NCT05704400)**
Evidence for FSGS more limited, heterogeneous FSGS phenotype: - *Remission rates are lower compared to MCD* - *Those not responding to other CNI/Steroids also less likely to respond*	

Obinutuzumab	
Sustained remission in children with steroid dependent/ frequently relapsing nephrotic syndrome, rituximab resistance or relapse with rituximab treatment.	**Ongoing/Planned Studies:** • **Phase 2 FSGS (Change in proteinuria at M6 & M12: NCT 04983888)** • **Phase 2/3 MCD (Incidence of relapse within 12 months: NCT05786768)**
Induced remission in adults with steroid dependent/frequently relapsing MCD, after various immunosuppression including rituximab.	
Induced remission in adults with frequently relapsing and treatment resistant (including rituximab) primary FSGS.	

Anti-CD38 (Daratumumab)

- **In combination with rituximab or after failing rituximab/Obinutuzumab**
- **Multi-drug resistant nephrotic syndrome**
- **Recurrence of FSGS after transplantation**

Results: We enrolled 8 patients: 5 with MRNS and 3 FSGSr (**Fig.1a**). MRNS resulted resistant to previous infusion of rituximab alone (last infusion at least 9 months before enrollment). Combined rituximab + daratumumab therapy induced CR or PR in 3 and 2 subjects with MRNS, respectively (**Fig.1b**). In one patient with older history of MRNS (5yrs), proteinuria remission was transient, but she refused a second treatment. All 3 FSGSr achieved CR/PR and PEX was stopped. Relapse occurred after 4 months in all pts. We repeated the combined treatment in 2 pts that after initial reduction, had a second relapse after 4 months. Thereafter, administration of daratumumab alone obtained remission as well (**Fig.1c**). Treatment was well tolerated and all patients are in active follow-up.