Top 10 Takeaways for Clinicians from the KDIGO 2021 Clinical Practice Guideline for the Management of Membranous Nephropathy

1 Diagnosis of membranous nephropathy (MN)

A kidney biopsy is not required to diagnose membranous nephropathy in a patient with nephrotic syndrome and a positive PLA2Rab test, but may help in determining prognosis and treatment decisions. (Figure 1)

2 Added value of kidney biopsy staining

A negative PLA2Rab test does not rule out PLA2R-associated MN. PLA2Rab can be absent in early disease. A positive glomerular staining of a kidney biopsy for PLA2R defines PLA2R-associated MN.

3 Be aware of new antigens

Identification of new antigens might help in defining the underlying cause in PLA2Rab negative patients.

4 Exclude secondary causes of MN

Evaluate all patients with MN for secondary causes such as infections, systemic diseases, malignancies, certain drugs (NSAIDs) or nutritional supplements (lipoic acid).

5 Prophylactic anticoagulant therapy

Patients with MN are at high risk of arterial and venous thromboembolic events. Prophylactic anticoagulant therapy is advised in patients with low serum albumin levels taking into account bleeding risk. (Figure 2)

6 Conservative therapy

All patients should receive optimal supportive therapy targeting edema, blood pressure, dietary salt intake, and lipid profile. Monitor the patient regularly, whilst evaluating risk parameters (see below). The duration of conservative therapy might vary with risk levels and response.

7 Risk-based immunosuppressive therapy

Start of and the choice of immunosuppressive drugs are guided by risk evaluation based on a combination of change in serum creatinine, serum albumin, and proteinuria. (Figure 3) When available, serum PLA2Rab levels, urine protein selectivity index, and excretion of low molecular weight proteins provide added value.

8 Immunological monitoring

Whilst clinical remission is the goal of therapy, immunological response precedes clinical response by several months. In patients with PLA2Rab positive MN, regular assessment of PLA2Rab after start of therapy enables early evaluation of treatment response and provides guidance for treatment change.

9 Treatment resistance

Lack of clinical response after several lines of therapies defines resistance, and patients should be referred to an expert center to discuss additional therapy. Residual proteinuria per se is not a sign of active MN, and especially in patients with immunological remission or normalized serum albumin levels, secondary FSGS must be excluded.

10 Kidney transplantation

Evaluation of PLA2Rab and if necessary PLA2R-antigen aids in predicting post-transplant recurrence. In patients with recurrent MN and proteinuria >1 g/day, rituximab is effective therapy. (Figure 4)

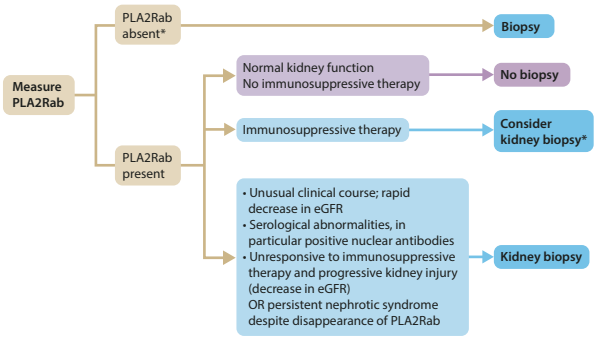

Figure 1

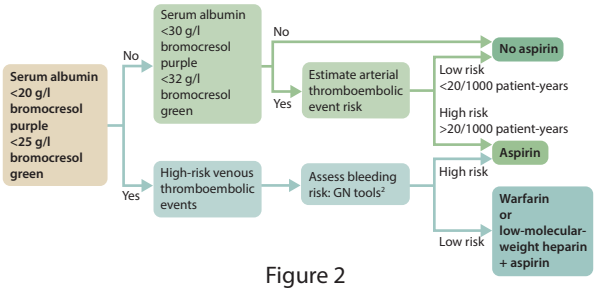

Figure 2

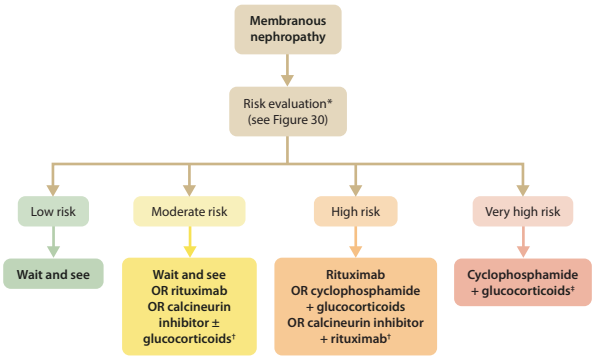

Figure 3

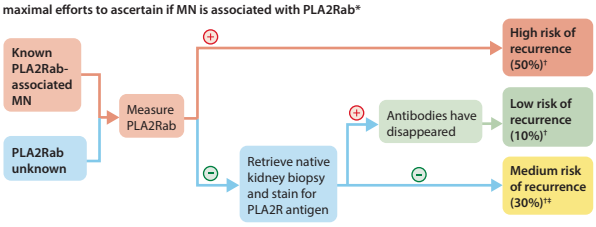

Figure 4

FSGS, focal segmental glomerulosclerosis; NSAIDS, nonsteroidal anti-inflammatory drugs; PLA2Rab, M-type phospholipase A2 receptor antibody