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ANTIGEN PROFILING

Move beyond "primary vs secondary" MN –
An antigen-based classification guides evaluation and prognosis.

ANTIGEN	ASSOCIATIONS / NOTES
PLA2R (~70–80%) 	- Classic primary MN - Strong association with malignancy - Titres correlate with disease activity
THSD7A (~5–10%) 	- More common in females - Often malignancy associated
NELL1 (~3–5%) 	- Frequently malignancy associated - May occur with PLA2R
EXT1 / EXT2 (<2%) 	- Genetic associations - Often younger patients
Others Sema3B, PCDH7, NTNG1, HTRA1, NCAM1, etc. 	- Antigen discovery is evolving - Comprehensive testing in seronegative MN



Know the antigen — Look for the association —
Guide the evaluation

2

RISK STRATIFICATION

Integrate clinical parameters with anti-PLA2R titre/kinetics.
Stratify risk to decide timing and intensity of therapy.

	KEY FEATURES
 LOW RISK Low risk of progression	- Proteinuria <3.5 g/day - Normal albumin - Stable eGFR - Low / negative anti-PLA2R
 MODERATE RISK Intermediate risk	- Proteinuria 3.5–8 g/day - Albumin 2.5–3.0 g/dL - Stable or slowly ↓ eGFR - Rising or persistent anti-PLA2R
 HIGH RISK High risk of progression	- Proteinuria >8 g/day - Albumin <2.5 g/dL - eGFR ↓ or declining - High and persistent anti-PLA2R
 VERY HIGH RISK Very high risk of kidney failure	- Nephrotic syndrome + eGFR <60 - Rapid eGFR decline - Very high / rising anti-PLA2R

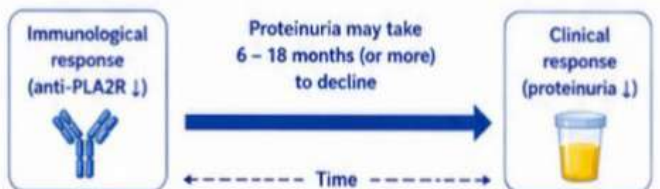


Treat the patient, the risk and the antibody –
not proteinuria alone.

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RESISTANT MEMBRANOUS NEPHROPATHY

Differentiate persistent proteinuria from true immunological resistance.



TRUE IMMUNOLOGICAL RESPONSE

- Anti-PLA2R falls to low / negative
- Even if proteinuria persists
- Continue therapy / observe
- Remission likely with time

TRUE RESISTANCE

- Persistent high / rising anti-PLA2R despite adequate therapy
- Lack of immunological response
- Consider change / intensification of therapy

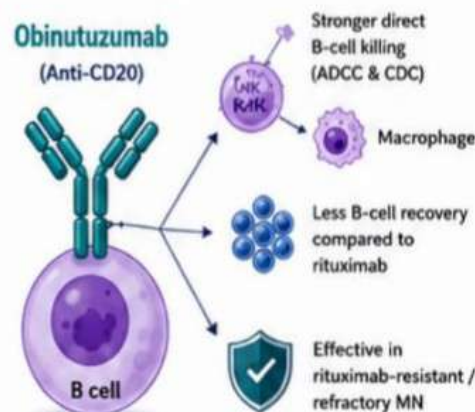


Monitor anti-PLA2R titres at baseline and serially –
The antibody is the best early marker of response.

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EVOLVING B CELL THERAPIES – OBINUTUZUMAB

A type-II anti-CD20 monoclonal antibody with potent B-cell depletion.



EVIDENCE SO FAR

2026 multicentre cohort
(refractory MN)

89.3%
Overall clinical response

82.1%
Achieved anti-PLA2R
≤ 2 RU/mL



Promising option in resistant MN.
More RCTs and long-term data awaited.

TAKE-HOME MESSAGES



Identify the antigen

It refines diagnosis and guides search for associated conditions.



Stratify the risk

Use proteinuria, albumin, eGFR trend and anti-PLA2R titre/kinetics.



Monitor the antibody

Immunological remission precedes clinical remission – be patient, be precise.



Address true resistance

Look at the antibody, not just the proteinuria.



Evolving therapies

B-cell targeted options like Obinutuzumab are expanding our armamentarium.



Antigen-driven approach • Risk-adapted therapy • Early immunological targets • Better outcomes

