

History in Nephrology

***True Legends are immortal through their deeds
and memories.!***

Advances in Membranous Nephropathy

Dr. Claudio Ponticelli



Claudio Ponticelli

1936 – 2026



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A PIONEER IN GLOMERULAR DISEASE
AND IMMUNOSUPPRESSIVE THERAPY

“Evidence, not dogma...”



Clinician
Scientist



Innovator in
Glomerular
Research



Mentor &
Teacher



Patient
Advocate

MAJOR CONTRIBUTIONS



PIONEERED MANAGEMENT OF GLOMERULAR DISEASES

Improved understanding and treatment strategies for membranous nephropathy, minimal change disease, IgA nephropathy, and nephrotic syndrome.



DEVELOPER OF THE PONTICELLI REGIMEN

Introduced and refined the **alternating** regimen of **steroids and alkylating agents** (cyclophosphamide/chlorambucil) that improved outcomes in membranous nephropathy and other glomerular diseases.



EVIDENCE-BASED APPROACH

Conducted landmark clinical trials that defined the role of immunosuppression in glomerular diseases and shaped international treatment guidelines.



PROLIFIC AUTHOR & THOUGHT LEADER

Authored more than 600 scientific publications and several influential books on nephrology and immunosuppressive therapy.



GLOBAL IMPACT

His work influenced generations of nephrologists worldwide and improved the lives of countless patients with kidney disease.



MENTOR TO GENERATIONS

Dedicated teacher and mentor who inspired young physicians through his wisdom, humility, and passion for nephrology.

LIFETIME OF DEDICATION

1936

Born in Italy

1960s

Began pioneering research in nephrology

1970s-1990s

Groundbreaking studies and clinical trials in glomerular diseases

2000s+

Continued research, writing, and mentorship worldwide

2026

Remembered as a legend in nephrology

HIS LEGACY LIVES ON

“
Evidence, not dogma...”





A MASTER.
A TEACHER.
A LEGEND.

Thank you, Prof. Claudio Ponticelli,
for a lifetime of contributions that
changed nephrology forever.

*A lasting inspiration
to all of us.* ✨



MEMBRANOUS NEPHROPATHY – KEY HIGHLIGHTS



From Antigen to Targeted Therapy

1 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.

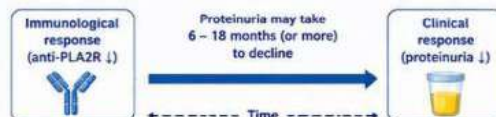
	KEY FEATURES
LOW RISK Low risk of progression	- Proteinuria <3.5 g/day - Normal albumin - Stable eGFR - Low / negative anti-PLA2R
MODERATE RISK Intermediate risk	- Proteinuria 3.5–8 g/day - Albumin 2.5–3.0 g/dL - Stable or slowly ↓ eGFR - Rising or persistent anti-PLA2R
HIGH RISK High risk of progression	- 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.

3 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

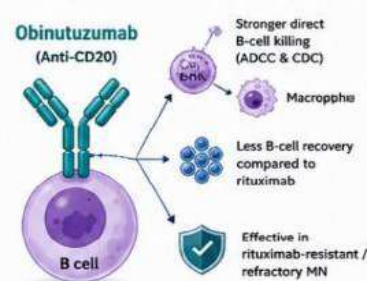
- Persistent high / rising anti-PLA2R despite adequate therapy
- Lack of immunological response
- Consider change / intensification of therapy



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

4 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