

How Urine Biomarkers Shape Eligibility Windows in Lupus Nephritis Trials

A practical look at using urine biomarkers to time screening, referral, and enrollment

Lupus nephritis enrollment problems often look operational from the outside. Sites miss enrollment windows, or patients screen positive on serology but cannot complete biopsy and confirmatory testing within the protocol's visit cadence. The upstream cause is usually the same: eligibility criteria written around a biomarker behavior that the disease does not actually exhibit.

Lupus nephritis flares are biologically unpredictable, and patients often feel well between flares. Ingrid van Rompaey, who led the project management for Worldwide's Phase III lupus nephritis program, has framed it directly:

“Patients don't feel immediately bad between flares. If we miss that window, we miss the chance to treat them.”

That is a description of how the disease behaves, not a comment on site performance. Protocols built for it from the outset enroll faster than those that aren't.

Getting that biology into the protocol is the first half of the work. The second half is operational. Patient education, monitoring cadence, referral pathways, site readiness, and central-lab turnaround determine whether the right patient reaches the site within the window defined by the protocol. That is the part a CRO can shape most directly.

The Traditional Biomarker Set Has Known Limits as a Window Definition

The standard serological set for SLE and lupus nephritis (i.e., anti-dsDNA antibodies, complement levels C3 and C4, and antinuclear antibody titers) shows disease activity at the population level. As gates for an enrollment window, they are noisy. A 2025 evidence review in *Life* concluded that traditional measures, including the protein-to-creatinine ratio and complement levels, have limited ability to [anticipate flares before they become clinically manifest](#).¹ The same body of work points to [emerging urinary candidates with promising predictive signals](#), including urinary CD163, IP-10 (CXCL10), and other proteins identified in longitudinal cohorts that rise weeks to months before a clinical flare.² These are early-stage tools. They are not yet routinely implemented in pivotal trials or widely available in clinical practice, and they read best as a complement to the established serological and urinary measures rather than a replacement for them.

Anti-dsDNA titers and complement alone are the wrong dial for an eligibility recheck. Patients with rising urinary inflammatory signals can pass through a screening visit with stable serology and exit the window before the next planned visit captures them. For sponsors defining an eligibility window, the practical question is which signal triggers a recheck and how often that recheck occurs. A window keyed to a predictive urinary signal, paired with a monitoring cadence frequent enough to catch the rise, gives sites a realistic chance of reaching the patient while they are still enrollable.

Patient Self-Monitoring Shortens the Path to the Screening Visit

The harder enrollment problem in lupus nephritis sits earlier in the patient journey. Once a patient arrives at the clinic, the diagnostic workup can begin promptly. Getting that patient to the clinic while the window is still open is the real work, and it depends on the patient recognizing early signs and acting on them. That is where education and patient-administered monitoring carry weight. Worldwide has used dipstick monitoring as an [early flare-detection tactic in rare-disease programs](#).³ Using a dipstick shortens the time between proteinuria onset and a sponsor-validated screening visit. A dipstick reads one analyte and misses the broader biology of a flare, so it works best as a referral trigger paired with confirmatory urine biomarker assays at the site visit.

Self-monitoring at home only pays off when the site can act on it quickly. Site responsiveness and referral routing fall between a patient noticing a change and confirmed enrollment, and include central-lab turnaround for the confirmatory assay. This is where an experienced CRO can add significant value by building the operational chain that turns an early at-home reading into a confirmed screening visit within the window.

Protocols built around dipstick-only confirmation tend to over-screen during stable periods and under-screen during the run-up to a flare. Protocols built around dipsticks plus a defined

urine biomarker panel (with serological context from anti-dsDNA and complement, plus IL-18 or type I interferon-regulated gene measures where stratification matters) [provide a broader biological window at the screening visit](#).³ For protocol design, the practical move is to write patient education and self-monitoring into the schedule as a defined referral path, with a named route from a home reading to a confirmatory site visit and a site team resourced to act on it quickly.

Biopsy & Screening Logistics Belong in Eligibility Design

Eligibility for lupus nephritis trials rests on more than a single biomarker reading. It includes biopsy timing, pathology review turnaround, changes to background medication, and other screening logistics, all of which shape whether a patient who screens in stays eligible through to randomization. A patient can meet the serological and urinary criteria and still fall out of the window while a biopsy is scheduled, and the pathology read comes back, or after a change in concomitant therapy shifts their disease activity.

Protocol design can directly plan for these realities. Sponsors can set biopsy and pathology timelines that align with the flare window and define upfront how any change in background medication is handled during screening. Site selection can then confirm that the chosen sites complete the biopsy-to-adjudication path within the eligibility period. Treating these logistics as part of eligibility design, rather than downstream operational detail, keeps more screened patients enrollable.

Eligibility Design Implications

The best eligibility criteria are not only scientifically sound but also operationally achievable. In lupus nephritis, protocol success depends on aligning disease biology with practical execution at the patient, site, and operational levels. Several protocol design choices consistently pay off across a lupus nephritis or SLE study.

The first is whether the eligibility window is

defined by a biomarker that predicts a flare or one that confirms it. These are different tests with different lead times, and the choice quietly determines how often patients arrive at the site visit already past the window.

The second choice is whether the assay panel is feasible at the sites the team has selected, with realistic central-lab turnaround times factored into the visit schedule. The Worldwide Optimizing Recruitment and Biomarker Precision in Autoimmune and Rare Autoimmune Trials white paper calls out the lack of [validated assays and heterogeneous clinical presentation as two recurring friction points in autoimmune enrollment](#).³

An eligibility panel that requires readouts taking days to return effectively narrows the protocol's window further than the protocol intended.

The third choice, and the one most likely to compress an enrollment window, is whether patient-administered monitoring is built in as a referral signal with a defined path to confirmation at the site visit. Dipsticks deliver real tactical value when the rest of the eligibility infrastructure can act on them within the flare window.

Evidence & Justification

Worldwide delivered the Phase III pivotal study that supported the first FDA-approved therapy for adult lupus nephritis. That study enrolled 358 patients across 240 sites in 27 countries and maintained its database lock schedule [despite natural disasters and unexpected medical events at sites in multiple regions](#).⁴ The constant was an eligibility design that treated lupus nephritis as a disease with narrow and biologically unpredictable activity windows, supported by site-level operations that recognized those windows in real time.

For sponsors planning a lupus nephritis or SLE trial, the design choice is not whether to use biomarkers. It is which biomarkers to use, at what cadence, how to pair them with patient-administered monitoring as a referral path, and how to resource sites to act on that signal inside the window. Our white paper, *Optimizing Recruitment and Biomarker Precision in Autoimmune and Rare Autoimmune Trials*, sets out the full framework and walks through the data behind each decision point.

Read the full [white paper](#). Or contact the Worldwide nephrology and autoimmune team to walk through your specific lupus nephritis or SLE protocol.

References

1. Vrabie A, Obrișcă B, Sorohan BM, Ismail G. Biomarkers in Lupus Nephritis: An Evidence-Based Comprehensive Review. *Life (Basel)*. 2025;15(10):1497. doi:10.3390/life15101497
2. Renaudineau Y, Chauveau D, Faguer S, et al. Urinary soluble CD163 is useful as a “liquid biopsy” marker in lupus nephritis at both diagnosis and follow-up to predict impending flares. *J Transl Autoimmun*. 2024;9:100244. doi:10.1016/j.jtauto.2024.100244
3. Worldwide Clinical Trials. *Optimizing Recruitment and Biomarker Precision in Autoimmune and Rare Autoimmune Trials*. White paper, May 2025 (revised April 2026). SLE biomarker section, friction points framework.
4. Worldwide Clinical Trials. *Lupus Nephritis Phase III Case Study*. Internal. Quote: Ingrid van Rompaey, PhD, Executive Director, Project Management, Rare Disease.