SIGNIFICANCE STATEMENT

About 80% of patients with primary membranous nephropathy (pMN) have PLA2R1 auto-antibodies (PLA2R1-Ab). Although Ab titers are associated with disease activity, predicting clinical outcome is challenging. In retrospective studies both high PLA2R1-Ab titer and PLA2R1 epitope spreading have correlated with poor outcome. This paper analyzes the predictive value of PLA2R1-Ab titer and epitope spreading in a prospective cohort of 58 patients treated with rituximab or control (GEM-RITUX). The results suggest that epitope spreading at baseline predicts a reduced likelihood of clinical remission independently of PLA2R1-Ab titer. We propose that epitope spreading be considered in the decision for early therapeutic intervention in pMN patients. These findings should be confirmed in larger cohorts of patients.