# Supplementary materials

# Four trajectories of 24-hour urine protein levels in real-world lupus nephritis cohorts

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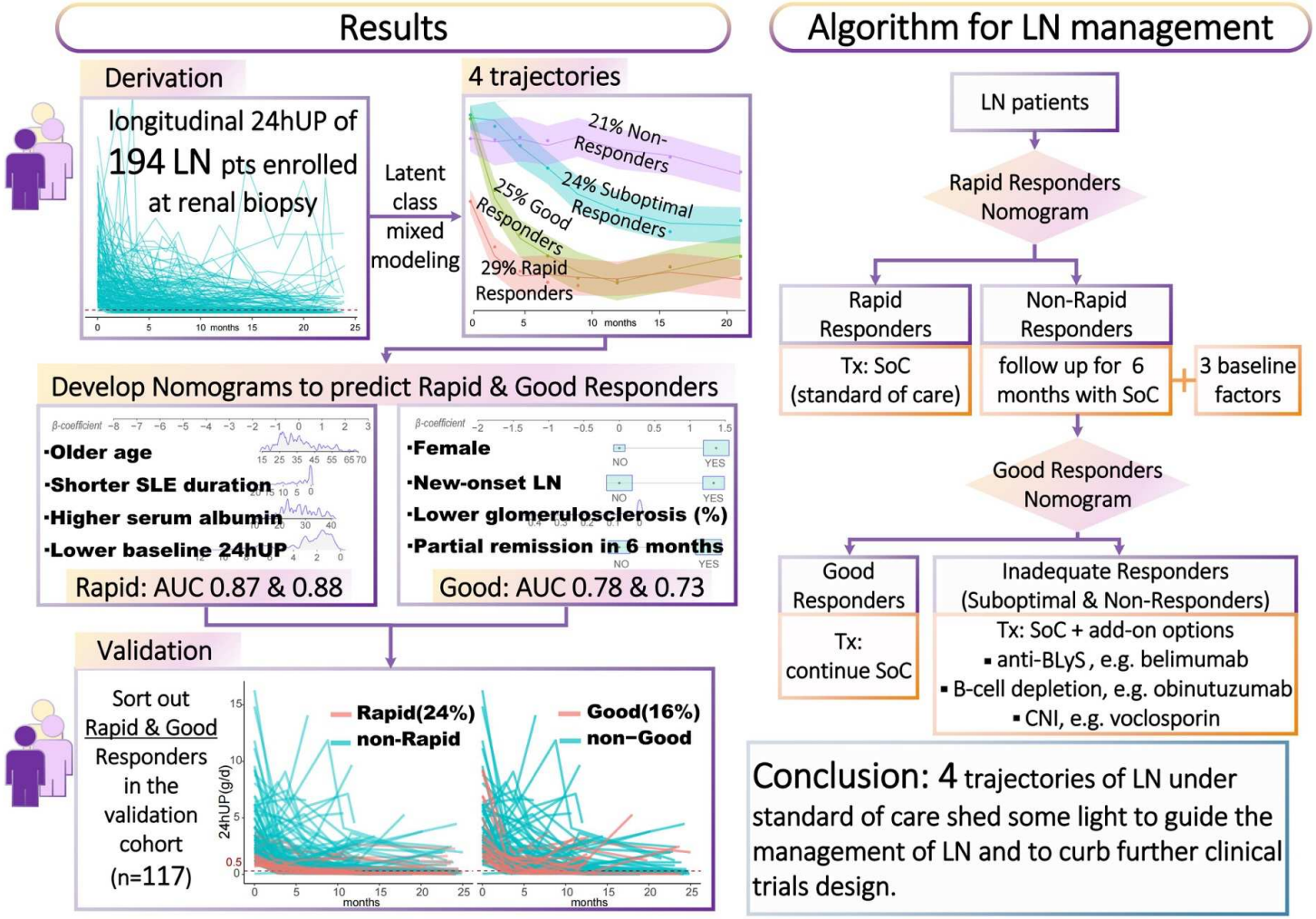
19 ● **GRAPHICAL ABSTRACT**

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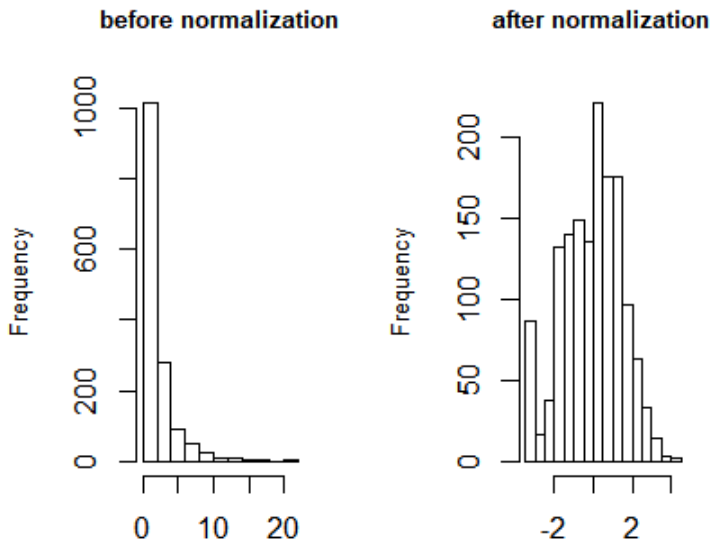
22 **1 LCMM process**

23 **1.1 Normalization of values of 24-hour urine protein(24hUP)**

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25 **Figure S1** The Box-Cox transformation was used to normalize the values of 24hUP.

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### 1.2 STEP 1 Standardized residual plots of fixed-effect model for each class adjusting the selection of a random-effect structure in the scoping model.

We constructed a scoping model using K=3 classes based on the clinical classification of response to LN treatment, namely complete response (CR), partial remission (PR) and no remission (NR). The **Figure S2** presented standardized residual plots for the 3 classes in a model with no random effects. The curved trajectories of 3 classes showed that a non-linear (quadratic or cubic) random model is desirable.

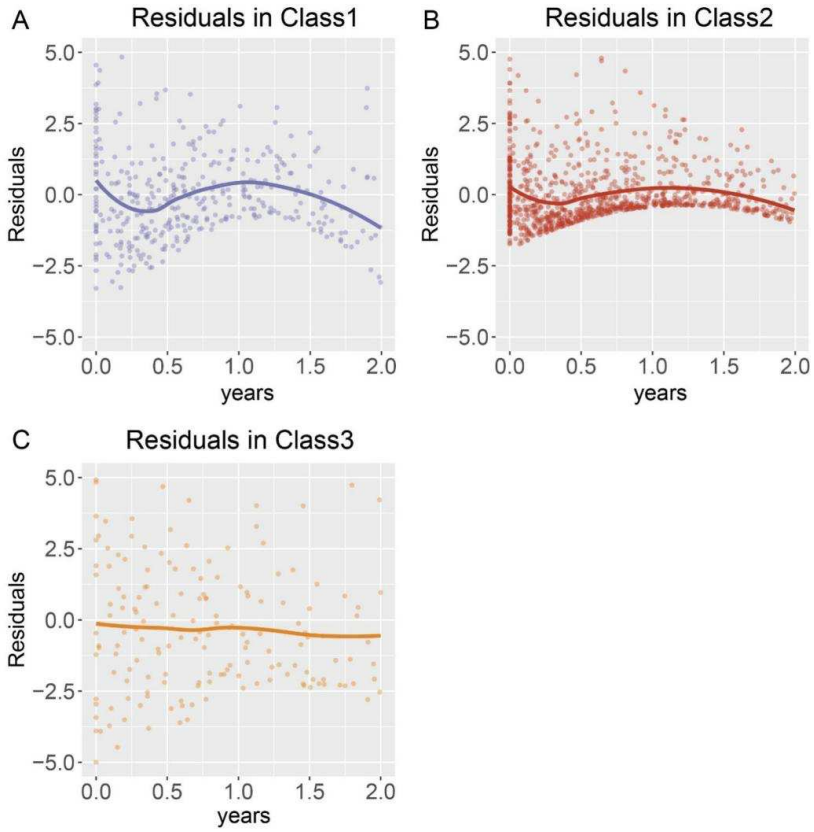



**Figure S2.** Standardized residual plots for the 3 classes in a model with no random effects.

### 1.3 STEP 2 Determine the optimal number of classes

To determine the optimal number of classes, we constructed a mixed effects model with latent classes K=1-10 using lcmm function with quadratic specification of time from the 'lcmm' package for R. The BIC and sizes of each latent class are presented in **Table S1**. The model with four classes was identified with the lowest BIC.

**Table S1**. BIC and classes percentages for models with 1 to 10 classes.

| G | loglik | npm | BIC | SABIC | entropy | %class1 | %class2 | %class3 | %class4 | %class5 | %class6 | %class7 | %class8 | %class9 | %class10 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | -3015.45 | 7 | 6067.77 | 6045.60 | 1.00 | 100.00 | | | | | | | | | |
| 2 | -2942.36 | 11 | 5942.67 | 5907.82 | 0.92 | 12.37 | 87.63 | | | | | | | | |
| 3 | -2911.57 | 15 | 5902.16 | 5854.65 | 0.94 | 11.86 | 3.61 | 84.54 | | | | | | | |
| 4 | -2891.13 | 19 | 5882.35 | 5822.16 | 0.90 | 11.86 | 1.55 | 73.71 | 12.89 | | | | | | |
| 5 | -2886.31 | 23 | 5893.78 | 5820.92 | 0.87 | 10.31 | 8.25 | 1.55 | 73.71 | 6.19 | | | | | |
| 6 | -2891.13 | 27 | 5924.49 | 5838.96 | 0.68 | 11.86 | 13.92 | 1.55 | 0.00 | 72.68 | 0.00 | | | | |
| 7 | -2891.13 | 31 | 5945.56 | 5847.36 | 0.78 | 11.86 | 1.55 | 0.00 | 0.00 | 12.89 | 73.71 | 0.00 | | | |
| 8 | -2879.85 | 35 | 5944.07 | 5833.19 | 0.74 | 10.82 | 3.09 | 1.55 | 10.31 | 0.00 | 1.55 | 72.68 | 0.00 | | |
| 9 | -2875.99 | 39 | 5957.42 | 5833.87 | 0.66 | 10.82 | 7.22 | 1.55 | 0.00 | 70.10 | 0.00 | 0.00 | 8.25 | 2.06 | |
| 10 | -2884.03 | 43 | 5994.57 | 5858.36 | 0.67 | 11.34 | 1.55 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 70.10 | 14.43 | 2.58 |

### 1.4 STEP 3 Refine the model

We further refined and compared models using the favored K=4 with different parameters: (i) using time, quadratic time^2 and cubic time^3; (ii) normalizing transformation of urine protein (**Figure S1**); (iii) using linear and beta splines. Model performances (BIC) and subjects' distributions in the latent classes were reported in the **Table S2**. Model with **unnormalized 24hUP, cubic time effects and beta splines** had lowest BIC and was used in the following analysis.

**Table S2.** BICs and subjects' distributions in each latent class were presented. Model with different parameters of data (24hUP normalized), time effects and splines

| normalization of urine protein | spline | time | loglik | npm | BIC | SABIC | entropy | %class1 | %class2 | %class3 | %class4 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| NO | linear | linear | -3035.73 | 15 | 6150.48 | 6102.96 | 0.81 | 7.22 | 2.58 | 90.21 | 0.00 |
| NO | linear | Quadratic | -2891.13 | 19 | 5882.35 | 5822.16 | 0.90 | 11.86 | 1.55 | 73.71 | 12.89 |
| NO | linear | Cubic | -2827.74 | 23 | 5776.64 | 5703.78 | 0.90 | 12.89 | 12.89 | 73.20 | 1.03 |
| NO | beta | linear | -2002.35 | 17 | 4094.26 | 4040.41 | 0.50 | 29.38 | 24.74 | 0.00 | 45.88 |
| NO | beta | Quadratic | -1834.70 | 21 | 3780.03 | 3713.51 | 0.69 | 12.37 | 34.02 | 17.01 | 36.60 |
| **NO** | **beta** | **Cubic** | **-1773.03** | **25** | **3677.76** | **3598.57** | **0.67** | **25.26** | **24.23** | **29.38** | **21.13** |
| YES | linear | linear | -2100.62 | 15 | 4280.26 | 4232.74 | 0.71 | 5.67 | 48.45 | 43.30 | 2.58 |
| YES | linear | Quadratic | -1942.58 | 19 | 3985.25 | 3925.06 | 0.64 | 13.40 | 40.21 | 11.34 | 35.05 |
| YES | linear | Cubic | -1896.81 | 23 | 3914.78 | 3841.92 | 0.62 | 17.53 | 37.11 | 18.04 | 27.32 |
| YES | beta | linear | -2087.25 | 17 | 4264.06 | 4210.21 | 0.73 | 50.00 | 5.67 | 41.75 | 2.58 |
| YES | beta | Quadratic | -1936.76 | 21 | 3984.14 | 3917.61 | 0.64 | 16.49 | 40.72 | 35.05 | 7.73 |
| YES | beta | Cubic | -1893.48 | 25 | 3918.65 | 3839.46 | 0.72 | 0.52 | 20.62 | 35.05 | 43.81 |

### 1.5 STEP 4 Model adequacy assessments

Model adequacy was determined by assigning each patient to a trajectory class based on the posterior probability. The average of the maximum posterior probability assignments (APPA) and odds of correct classification (OCC) for each class were presented in **Table S3**.

**Table S3. APPA and OCC in Latent classes.**

| Description | Number of classes | BIC | Relative entropy | Class-specific parameters | Cluster1 | Cluster2 | Cluster3 | Cluster4 |
|---|---|---|---|---|---|---|---|---|
| Random Cubic Beta | 4 | 3677.76 | 0.67 | n of patients (%) | 57(29.4) | 49 (25.3) | 47(24.2) | 41(21.1) |
| | | | | Average posterior probability assignment (APPA) | 0.837 | 0.798 | 0.752 | 0.843 |
| | | | | Odds of correct classification （ OCC） | 12.5 | 11.36 | 9.97 | 19.2 |

### 1.6 STEP 5 Graphical presentation

Graphical presentation approaches with the use of mean trajectory plots with 95% predictive intervals for each class and individual level ‘spaghetti plots’ were presented in Figure 1.

**Table S4. Detailed pathologic, laboratory features and detailed immunosuppressive agents for induction in four latent classes in the derivation cohort.**

| | | Rapid Responders | Good Responders | Suboptimal Responders | Non-Responders | p value |
|---|---|---|---|---|---|---|
| N (%) | | 57 (29.4) | 49 (25.3%) | 47 (24.2%) | 41 (21.1%) | |
| Karyorrhexis (%) | | 30(53.6)a | 37(80.4)b | 27(61.4) | 27(67.5) | 0.038 |
| Cell crescents | | 0.10(0.15)a | 0.18(0.20) | 0.22(0.22)b | 0.15(0.19) | 0.026 |
| Fibrous crescents | | 0.01(0.04) | 0.01(0.05) | 0.04(0.11) | 0.02(0.05) | 0.094 |
| Glomerulosclerosis | | 0.06(0.09)a | 0.05(0.12)a | 0.13(0.17)b | 0.06(0.11)a | 0.003 |
| Tubulointerstitial sclerosis (%) | | 24(43.6)b | 12(26.1)a | 24(57.1) | 15(37.5) | 0.028 |
| Tubular atrophy | | 2.50(4.86)a | 3.04(5.91)a | 8.52(13.36)b | 7.75(11.21) | 0.004 |
| Thrombotic microangiopathies (%) | | 8(14.5) | 12(26.1) | 9(20.5) | 7(17.5) | 0.52 |
| Wire loop (%) | | 25(44.6) | 29(64.4) | 26(59.1) | 21(52.5) | 0.219 |
| Fibrinoid necrosis (%) | | 10(17.9) | 17(37.0) | 17(38.6) | 9(22.5) | 0.054 |
| Fibrous crescents | | 0.01(0.04) | 0.01(0.05) | 0.04(0.11) | 0.02(0.05) | 0.094 |
| Pulse therapy (%) | | 0 (0) | 6(12.5) | 4(8.7) | 4(10.0) | 0.163 |
| Hemoglobin (g/L) | | 106.89(25.68) | 99.69(19.57) | 103.70(28.14) | 109.37(24.87) | 0.13 |
| Platelet (10^9/L) | | 196.14(76.52) | 204.35(92.97) | 188.81(84.69) | 221.17(93.86) | 0.473 |
| D-Dimer (mg/L) | | 1.00(1.05) | 2.32(3.95) | 1.44(1.75) | 1.90(1.86) | 0.054 |
| Erythrocyte sedimentation rate (mm/H) | | 38.30(31.89) | 40.30(31.09) | 38.68(34.96) | 46.05(35.12) | 0.546 |
| C-reactive protein (mg/L) | | 6.24(12.51) | 3.71(4.21) | 11.42(18.92) | 5.85(6.29) | 0.022 |
| Immunoglobulin G (g/L) | | 15.06(5.90)b | 11.17(6.10)a | 10.92(5.47)a | 13.45(10.36) | 0.001 |
| Number of immunosuppressants for induction | | 1.09(0.47)a | 1.39(0.76)a/b | 1.77(1.00)b | 2.63(1.55)c | <0.001 |
| First line immunosuppressant for | Cyclophosphamide | 17(29.8) | 32(65.3) | 23(48.9) | 15(36.6) | 0.021 |
| | Mycophenolate Mofetil | 29(50.9) | 12(24.5) | 16(34.0) | 17(41.5) | |

| | | | | | | |
|---|---|---|---|---|---|---|
| induction (%) | Azathioprine | 6(10.5) | 0(0.0) | 2(4.3) | 0(0.0) | |
| | Ciclosporin A | 0(0.0) | 0(0.0) | 1(2.1) | 1(2.4) | |
| | FK506 | 0(0.0) | 0(0.0) | 1(2.1) | 3(7.3) | |
| | Leflunomide | 0(0.0) | 0(0.0) | 1(2.1) | 1(2.4) | |
| | Others | 2 (3.5) | 3 (6.1) | 2 (4.1) | 2 (4.8) | |
| Second line immunosuppressant for induction (%) | Cyclophosphamide | 3(50.0) | 2(20.0) | 4(17.4) | 7(23.3) | |
| | Mycophenolate Mofetil | 0(0.0) | 3(30.0) | 12(52.2) | 7(23.3) | |
| | Azathioprine | 0(0.0) | 3(30.0) | 3(13.0) | 1(3.3) | 0.014 |
| | FK506 | 3(50.0) | 0(0.0) | 2(8.7) | 6(20.0) | |
| | Others | 0(0.0) | 2(20.0) | 2(8.7) | 9(30.0) | |
| Last Complete remission (g/d) | | 0.19(0.31) | 0.36(0.46) | 1.06(1.08) | 2.04(1.60) | <0.001 |
| Last estimated glomerular filtration rate (mL/min/1.73m2) | | 104.83(23.71) | 109.31(19.68) | 93.76(34.53) | 86.66(40.93) | 0.069 |

Comparisons between each two groups were adjusted by Bonferroni test, and significant difference was noted by letter a, b or c; Different letters between two groups indicate significance, while the same letter or absence of letter indicates no difference.

Pulse therapy, MP more than 500mg.

**Table S5. Multinomial logistic regression models of baseline variables associated with either 'Good Responders', 'Suboptimal Responders' compared to 'Non-Responders'.**

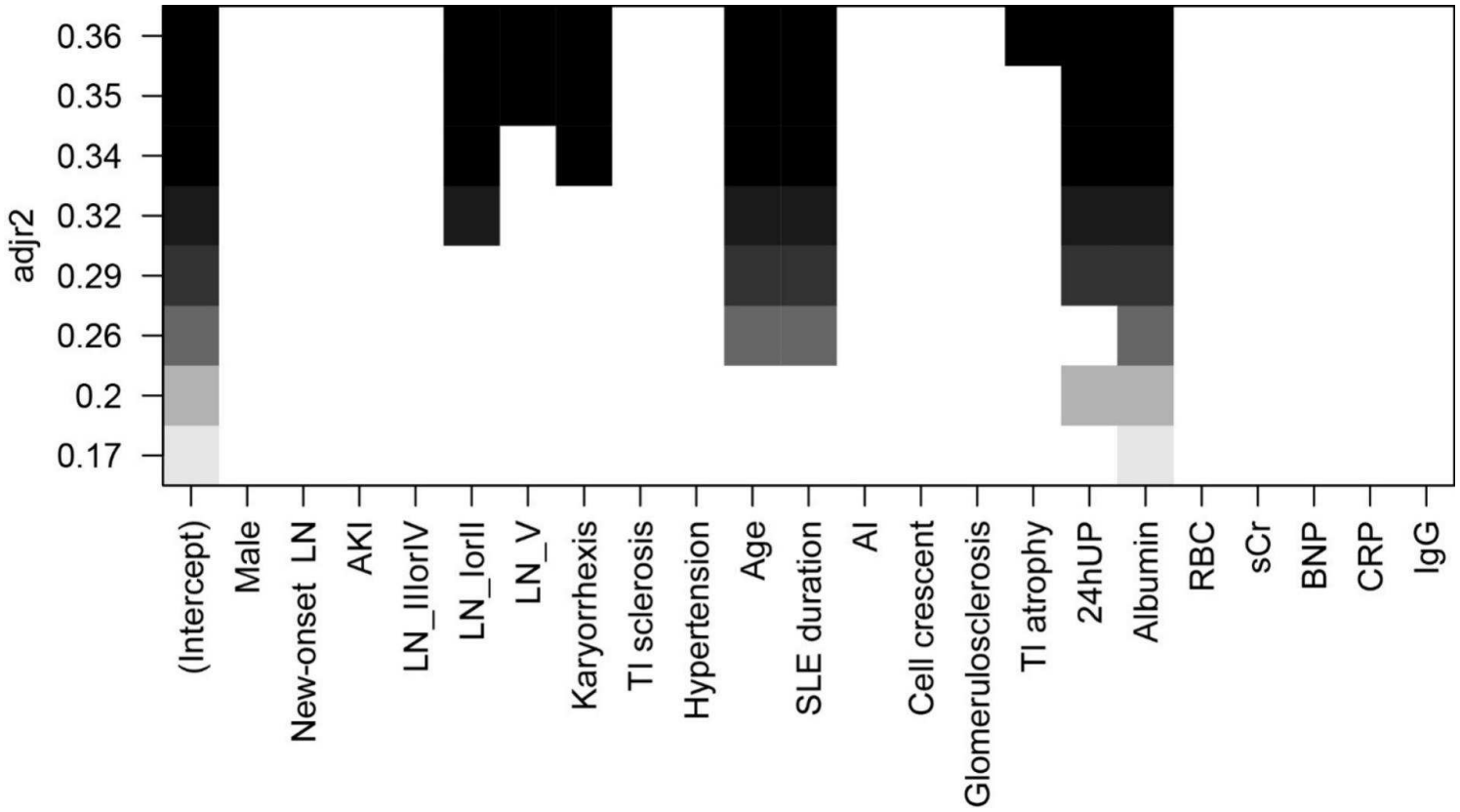
| | Good Responders | | Suboptimal Responders | |
|---|---|---|---|---|
| | OR (95%CI) | p value | OR (95%CI) | p value |
| Age/y | 0.98(0.93,1.04) | 0.562 | 1(0.95,1.05) | 0.922 |
| Male (ref: female) | 1.78(0.53,6.05) | 0.354 | 0.27(0.06,1.29) | 0.101 |
| SLE duration/y | 1.05(0.94,1.19) | 0.377 | 1.08(0.95,1.23) | 0.256 |
| New-onset LN (%) | 0.7(0.23,2.13) | 0.527 | 3.87(1.13,13.29) | 0.032 |
| Acute kidney injury (%) | 1.5(0.32,7.09) | 0.608 | 0.62(0.13,3.02) | 0.554 |
| LN class (%) Mixed | ref | / | ref | / |
| LN class (%) I or II | / | / | / | / |
| LN class (%) III or IV | 1.62(0.5,5.27) | 0.425 | 2.17(0.67,7.07) | 0.198 |
| LN class (%) V | 0.9(0.15,5.33) | 0.909 | 4.25(0.56,32.12) | 0.161 |
| Activity index | 1.02(0.88,1.18) | 0.775 | 1.05(0.91,1.21) | 0.518 |
| Karyorrhexis (%) | 0.56(0.12,2.59) | 0.46 | 7.14(1.3,39.31) | 0.024 |
| Cell crescents | 4.22(0.33,54.24) | 0.269 | 0.05(0,0.66) | 0.023 |
| Glomerulosclerosis | 252.44(25.94,2456.36) | <0.001 | 11.19(1.09,115.29) | 0.042 |
| Tubular atrophy | 0.98(0.92,1.03) | 0.37 | 0.95(0.88,1.02) | 0.144 |
| Tubulointerstitial sclerosis (%) | 1.37(0.31,6.14) | 0.679 | 2.21(0.43,11.32) | 0.34 |
| 24-hour urine protein (g/d) | 1.18(0.97,1.44) | 0.095 | 1.09(0.88,1.33) | 0.434 |
| Albumin (g/L) | 0.95(0.88,1.03) | 0.231 | 0.88(0.8,0.97) | 0.009 |
| Urine red blood cell/HP | 1.02(0.99,1.05) | 0.2 | 1.03(1,1.06) | 0.061 |
| Serum creatinine (umol/L) | 0.99(0.98,1) | 0.146 | 1(0.99,1.01) | 0.786 |
| Brain natriuretic peptide (pg/ml) | 1(1,1) | 0.156 | 1(1,1) | 0.819 |
| C-reactive protein (mg/L) | 1.02(0.98,1.07) | 0.306 | 0.92(0.83,1.02) | 0.095 |
| Immunoglobulin G (g/L) | 0.99(0.91,1.07) | 0.725 | 0.99(0.92,1.08) | 0.869 |
| Hypertension (%) | 0.62(0.22,1.77) | 0.377 | 0.62(0.21,1.87) | 0.396 |

1 **4 Table S6. Comparison of baseline characteristics between 'Rapid Responders' and non-'Rapid Responders' in derivation cohort**

| | | Rapid Responders | Non-'Rapid Responders' | p value |
|---|---|---|---|---|
| N (%) | | 57(29.4%) | 137(70.6%) | |
| Age (y) | | 39.60(12.75) | 33.14(11.12) | 0.001 |
| Male (%) | | 7(12.3) | 25(18.2) | 0.419 |
| SLE duration (y) | | 3.69(5.61) | 4.88(5.43) | 0.17 |
| New-onset LN (%) | | 40(70.2) | 82(59.9) | 0.233 |
| Acute kidney injury (%) | | 7(12.3) | 49(35.8) | 0.002 |
| LN class (%) | I or II | 5(8.8) | 1(0.7) | |
| | III or IV | 32(56.1) | 58(42.3) | |
| | Mixed | 11(19.3) | 57(41.6) | 0.001 |
| | V | 9(15.8) | 21(15.3) | |
| Activity index | | 7.51(5.09) | 10.65(5.64) | <0.001 |
| Karyorrhexis (%) | | 31(54.4) | 97(70.8) | 0.042 |
| Cell crescents | | 0.10(0.15) | 0.18(0.20) | 0.009 |
| Glomerulosclerosis | | 0.06(0.09) | 0.08(0.14) | 0.227 |
| Tubular atrophy | | 2.72(5.09) | 6.35(10.77) | 0.016 |
| Tubulointerstitial sclerosis (%) | | 26(45.6) | 54(39.4) | 0.523 |
| 24-hour urine protein (g/d) | | 1.65(1.24) | 4.49(3.55) | <0.001 |
| Albumin (g/L) | | 30.92(5.44) | 25.29(6.34) | <0.001 |
| Urine red blood cell/HP | | 15.90(37.46) | 20.40(27.42) | 0.353 |
| Serum creatinine (umol/L) | | 69.33(31.27) | 101.89(68.02) | 0.001 |
| Brain natriuretic peptide (pg/ml) | | 96.78(207.30) | 280.25(644.93) | 0.037 |
| C-reactive protein (mg/L) | | 6.24(12.51) | 7.10(12.23) | 0.659 |
| Immunoglobulin G (g/L) | | 14.93(5.85) | 11.91(7.49) | 0.007 |
| Hypertension (%) | | 18(31.6) | 75(54.7) | 0.005 |

2

**Figure S3. All subset regression showed best combination of variables with 1-8 variables allowed to be enrolled to predict 'Rapid Responders'.**



**6 Table S7. Prediction models for 'Rapid Responders' in LN.**

| | Factors# | Model 1 | | | Model 2 | | | Model 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | β | Odds Ratio (95% CI) | p value | β | Odds Ratio (95% CI) | p value | β | Odds Ratio (95% CI) | p value |
| Clinical features | Age/y | 0.07 | 1.07(1.03-1.13) | 0.001 | 0.08 | 0.19 (0.03~0.91) | 0.001 | 0.08 | 1.09 (1.04-1.14) | <0.001 |
| | SLE duration/y | -0.15 | 0.86(0.76-0.94) | 0.004 | -0.12 | 0.21 (0.03~1.14) | 0.03 | -0.12 | 0.89 (0.78-0.96) | 0.04 |
| | Albumin(g/L) | 0.16 | 1.18(1.10-1.28) | <0.001 | 0.11 | 0.07 (0.008~0.38) | 0.01 | 0.12 | 1.12 (1.02-1.24) | 0.01 |
| | 24-hour urine protein (g/d) | | | | -0.5 | 0.6(0.41-0.81) | 0.003 | -0.51 | 0.60 (0.4-0.82) | 0.004 |
| | LN mix | | | | | | | ref | ref | ref |
| | LN I or II | | | | | | | 17.03 | 2.4*10e7 (NA) | 0.99 |
| | LN III or IV | | | | | | | -0.49 | 0.61(0.17-2.06) | 0.43 |
| | LN V | | | | | | | -0.45 | 0.64(0.13-2.80) | 0.56 |
| C-index | Training set | | 0.83 (0.75-0.91) | | | 0.87 (0.8-0.94) | | | 0.88 (0.81-0.95) | |
| | Testing set | | 0.76 (0.64~0.88) | | | 0.88 (0.79-0.96) | | | 0.86 (0.76-0.95) | |

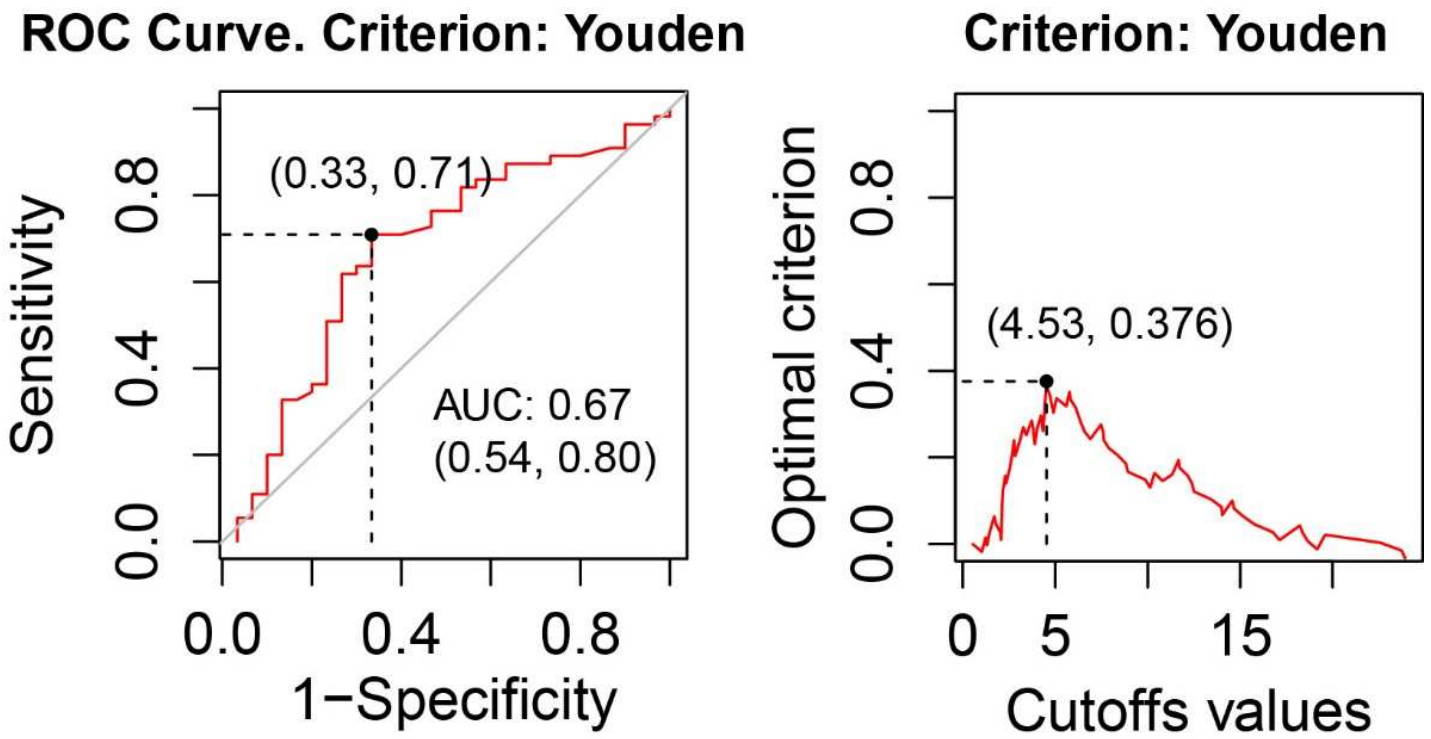
# Optimal cutoff values of age, SLE duration, albumin and 24hUP for differentiating 'Rapid Responders' from no were 48 years, 0.92 years, 25.7 g/L and 2.4 g/d. Of note, the univariate AUC of 24hUP was as high as 0.8 in discriminating 'Rapid Responders' form non-'Rapid Responders'. For those whose baseline 24hUP more than 2.4 g/d, 93% of them were turned out to be non-'Rapid Responders', indicating 24hUP as a valuable factor with excellent negative prediction value (NPV). Meanwhile, for patients with baseline 24hUP less than 2.4g/d, 56% were 'Rapid Responders'.

**Table S8. Prediction models for Good Responders in dataset with 'Rapid Responders' excluded. The C-indices were not satisfactory.**

| Factors | | Model 1 | | | Model 2 | | | Model 3 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Various | | β | Odds Ratio (95% CI) | p value | β | Odds Ratio (95% CI) | p value | β | Odds Ratio (95% CI) | p value |
| Clinical features | Gender/male | -1.5 | 0.22(0.03- 0.95) | 0.070 | -1.39 | 0.25(0.035-1.11) | 0.10 | -1.64 | 0.19 (0.03-0.92) | 0.064 |
| | New-onset LN (%) | 1.28 | 3.60(1.32-10.7) | 0.015 | 1.26 | 3.54 (1.26-10.94) | 0.02 | 1.37 | 3.94 (1.37-12.67) | 0.015 |
| | Glomerulosclerosis | -3.93 | 0.02 (0.00-1.13) | 0.093 | -4.57 | 0.01 (0.00-0.74) | 0.07 | -5.83 | 0.00 (0.00-0.32) | 0.037 |
| | Urine red blood cell/HP | | | | 0.02 | 1.01 (1.00-1.04) | 0.10 | 0.02 | 1.02(1.00-1.04) | 0.063 |
| | Age/y | | | | | | | 0.04 | 1.04(0.99-1.085) | 0.104 |
| C-index | Training set | | 0.755 (0.650-0.861) | | | 0.783 (0.679-0.887) | | | 0.778(0.672-0.885) | |
| | Testing set | | 0.665 (0.516-0.814) | | | 0.642 (0.484-0.80) | | | 0.646(0.487-0.805) | |

Delong test showed there was no difference between model 1 and model 2.

**Figure S4. AUC of PR months was 0.67 and optimal cutoff value of PR months in the training set was 4.53. PR within 6 months was chosen as a cutoff value for clinical convenience.**




For PR patients, time to PR was defined as time to first recorded PR, and time to first CR was used as a surrogate for CR patients without previously recorded PR. For NR patients, time of last visit was used for imputation.

**10 Figure S5. All subset regression showed best combination of variables with 1-8 variables allowed to be enrolled to predict 'Good Responders'. (PR within 6 mons involved)**

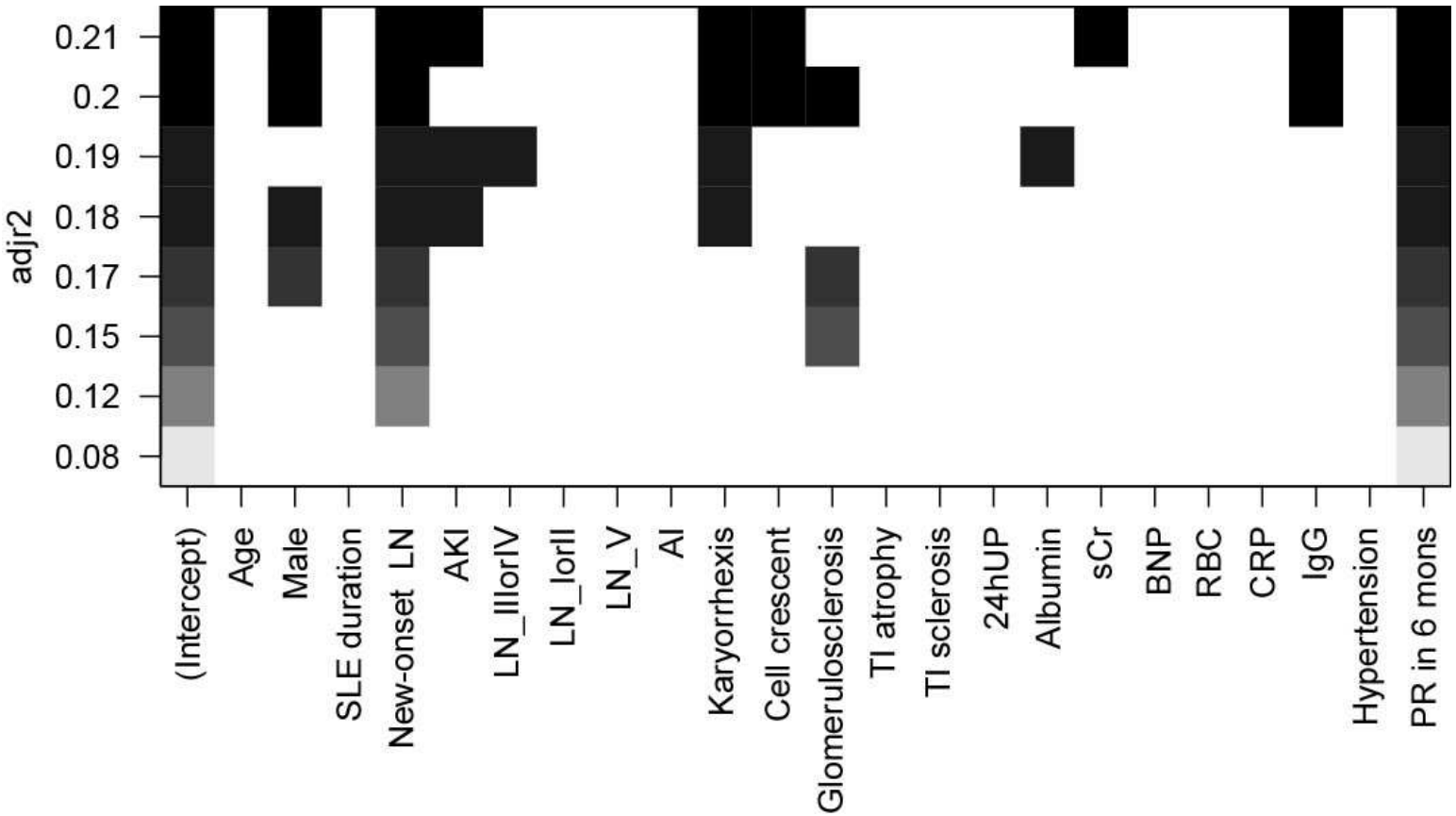


**Table S9. Final prediction models for 'Good Responders' with 4 variables.**

| Factors | | Model | | |
|---|---|---|---|---|
| | Various | β | Odds Ratio (95% CI) | p |
| Clinical features | Gender/female | 1.37 | 3.88(0.84-28.46) | 0.115 |
| | New-onset LN (%) | 1.24 | 3.45 (1.22-10.73) | 0.024 |
| | Glomerulosclerosis | -3.77 | 0.02 (0.00-1.45) | 0.113 |
| | PR within 6 mons (%) | 1.19 | 3.29(1.19-9.73) | 0.024 |
| C-index | Training set | | 0.782 (0.680-0.885) | |
| | Testing set | | 0.730 (0.585-0.876) | |

**12 Table S10. Comparison of baseline features between derivation cohort with validation cohort.**

| | | Derivation Cohort | Validation Cohort | p value |
|---|---|---|---|---|
| n | | 194 | 117 | / |
| Follow-up/mon | | 17.50[12.17,21.65] | 18.00[12.30,23.70] | 0.032 |
| Age/y | | 35.04(11.96) | 34.03(11.22) | 0.465 |
| Male (%) | | 32(16.5) | 8(6.8) | 0.022 |
| SLE duration/y | | 4.53(5.50) | 5.13(6.04) | 0.079 |
| New-onset LN (%) | | 122(62.9) | 57(48.7) | 0.02 |
| LN class (%) | I or II | 6(3.1) | 3(2.6) | 0.936 |
| | III | 34(17.5) | 17(14.5) | |
| | IV | 56(28.9) | 33(28.2) | |
| | mix | 68(35.1) | 43(36.8) | |
| | V | 30(15.5) | 21(17.9) | |
| Glomerulosclerosis | | 0.07(0.13) | 0.07(0.13) | 0.512 |
| Albumin (g/L) | | 26.94(6.60) | 28.83(5.95) | 0.014 |
| 24-hour urine protein (g/d) | | 3.66(3.32) | 3.42(2.79) | 0.795 |
| Estimated glomerular filtration rate ($mL/min/1.73m^2$) | | 91.65(36.01) | 105.65(32.03) | 0.002 |
| Serum creatinine (umol/L) | | 91.44(60.44) | 74.09(55.88) | <0.001 |
| Complete remission (%) | | 110(56.7) | 70(59.8) | 0.566 |
| Time to Complete remission /mons | | 7.30(5.59) | 7.85(6.05) | 0.581 |
| Last estimated glomerular filtration rate （mL/min/1.73m2） | | 99.44(31.09) | 107.08(27.04) | 0.023 |

ACEI/ARB, Angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor antagonist (ARB); eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease.

**13 Figure S6. Spaghetti plot in the validation cohort. 'Rapid Responders' (red) were distinguished by nomogram developed in derivation cohort. Most of 'Rapid Responders' reached 0.5 very quickly.**

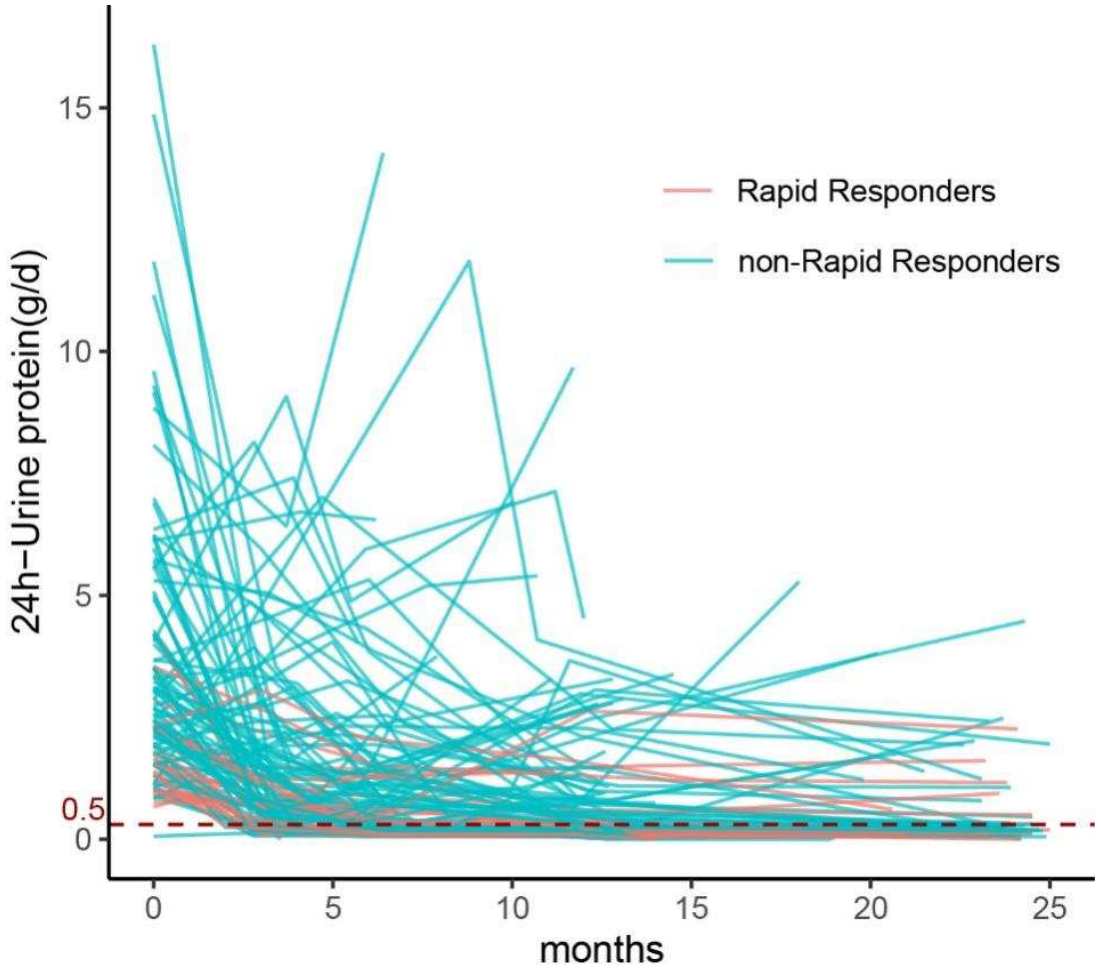


**Figure S7. Spaghetti plot in the validation cohort. 'Good Responders' (red) were distinguished by nomogram developed in derivation cohort.**

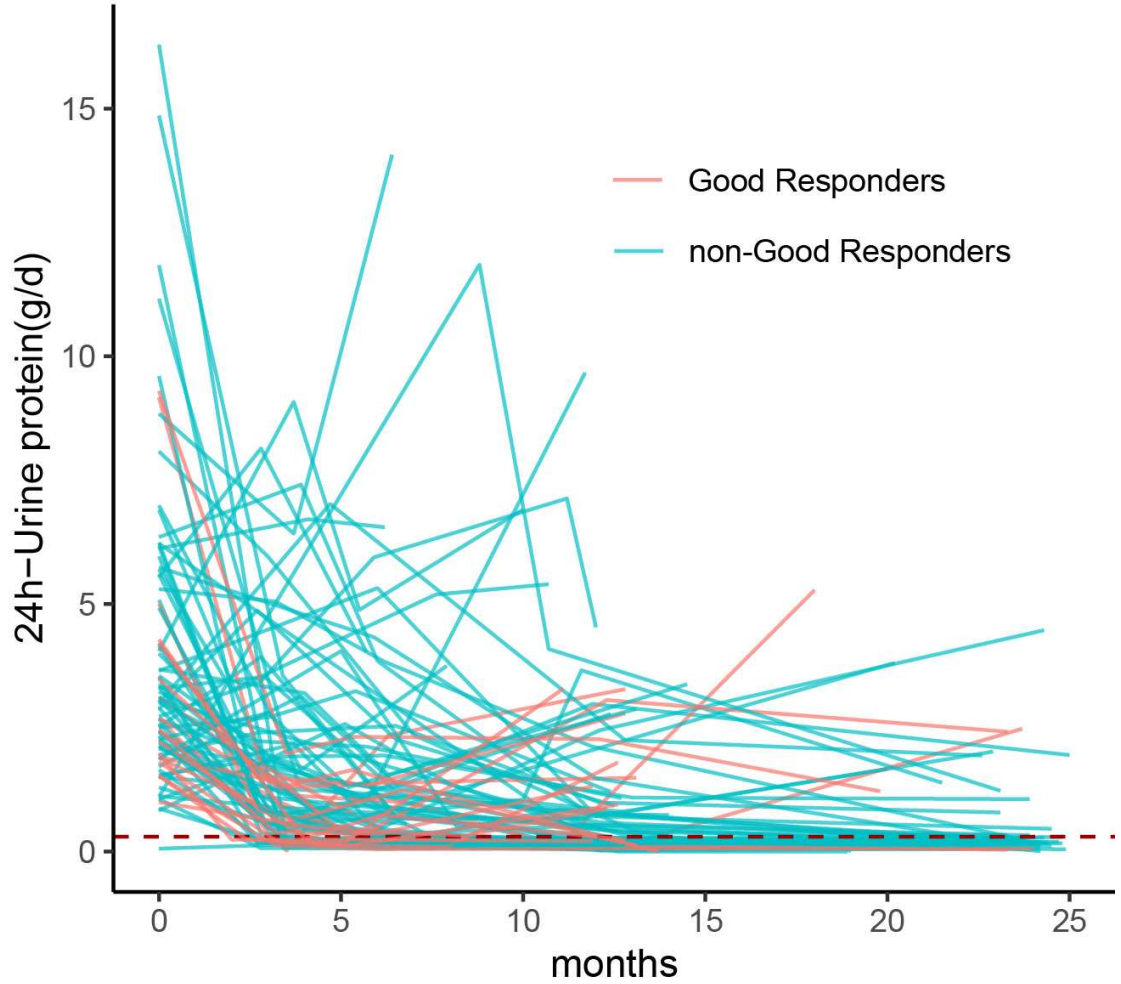
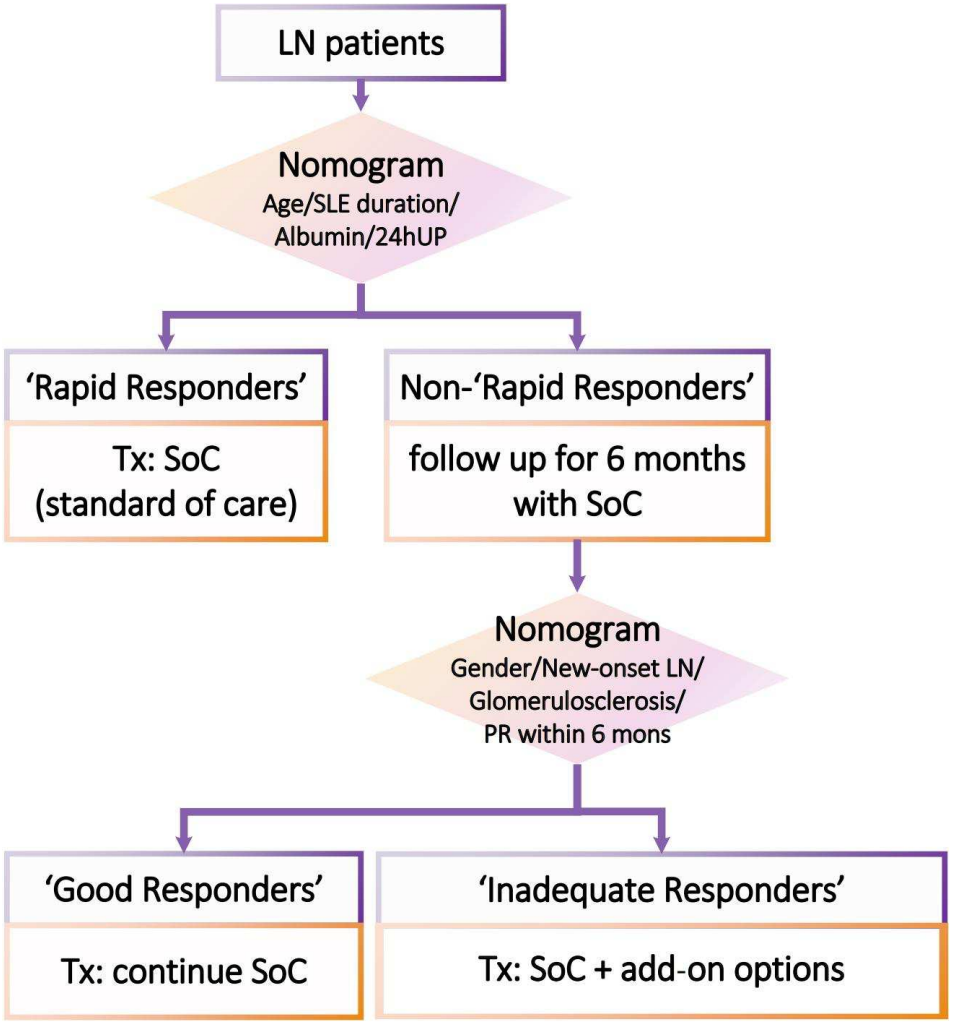



**Figure S8. Provisional treatment algorithm.**