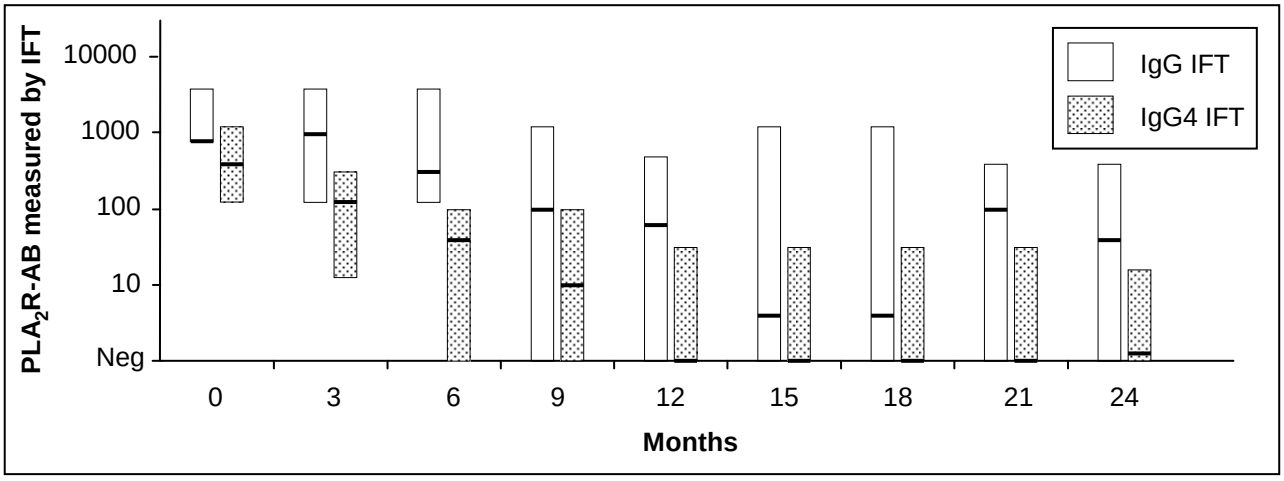
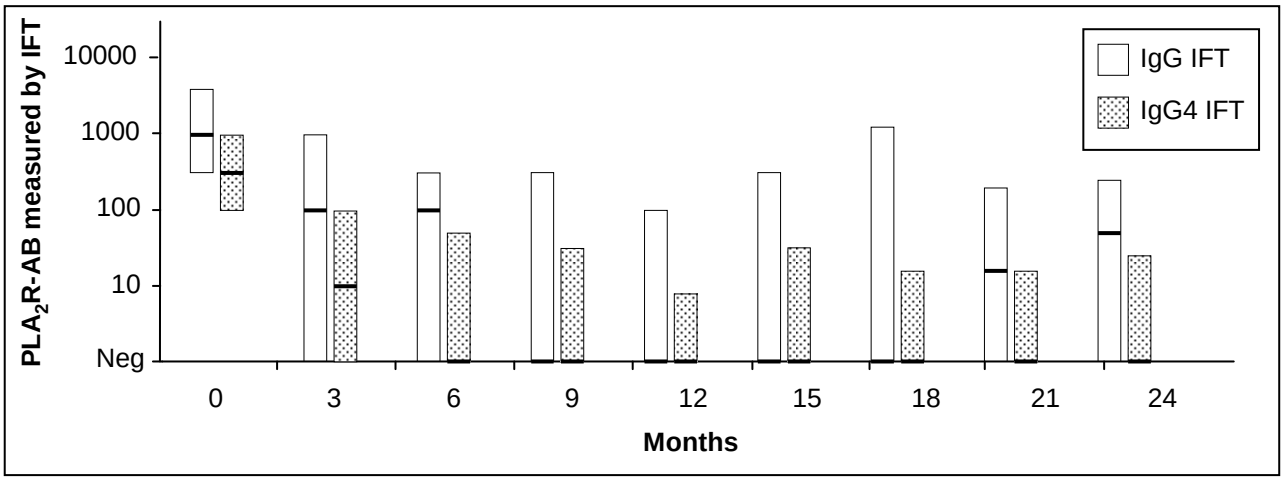
Supplemental Figure 1

A



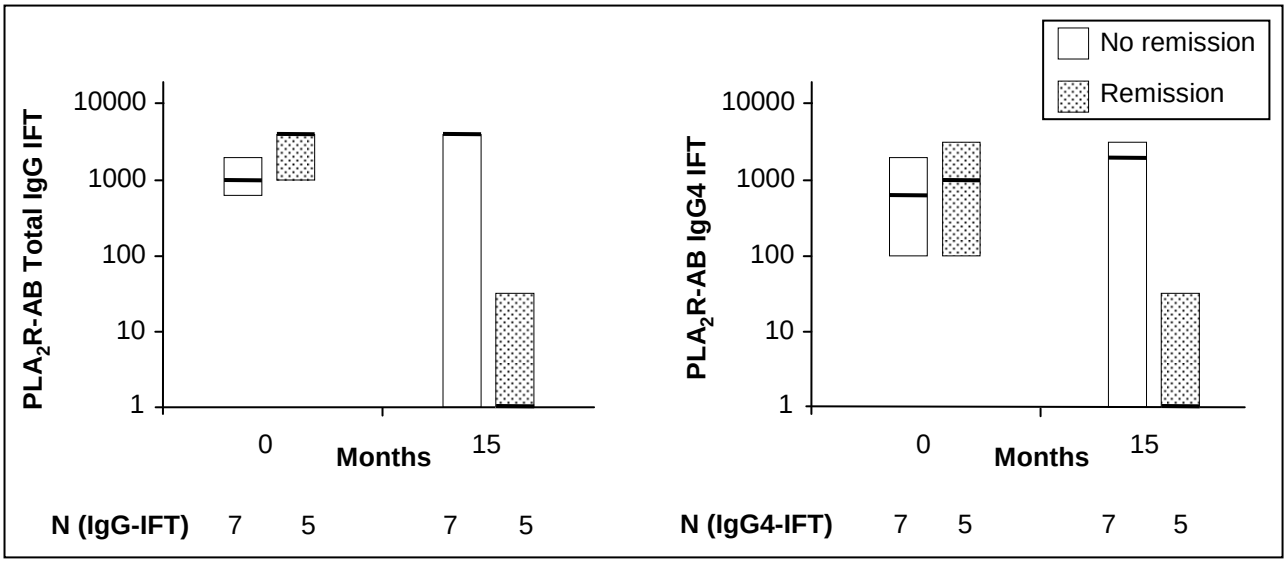
N (IgG-IFT)	133	108	99	96	84	66	48	33	25
N (IgG4-IFT)	128	107	99	95	84	64	48	33	24

B



N (IgG-IFT)	97	89	73	66	58	41	28	16	15
N (IgG4-IFT)	94	87	72	64	58	40	28	16	14

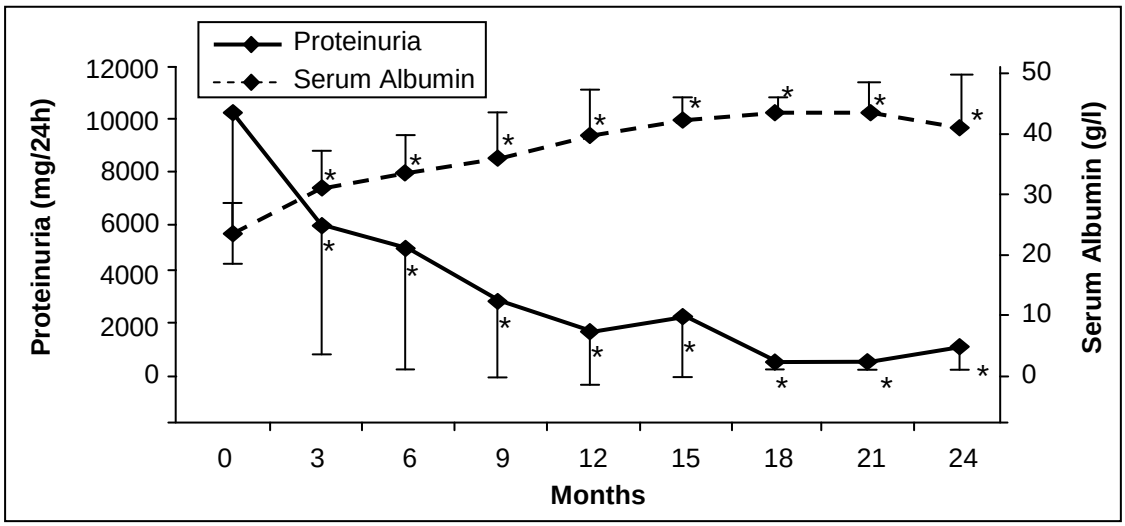
C



N (IgG-IFT)	7	5	7	5
N (IgG4-IFT)	7	5	7	5

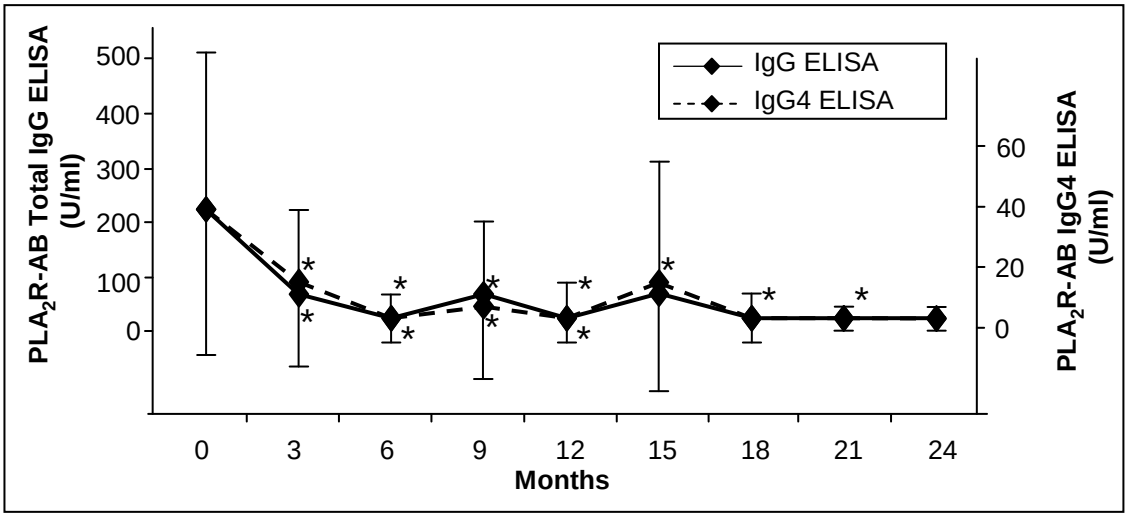
Supplemental Figure 2

Ai



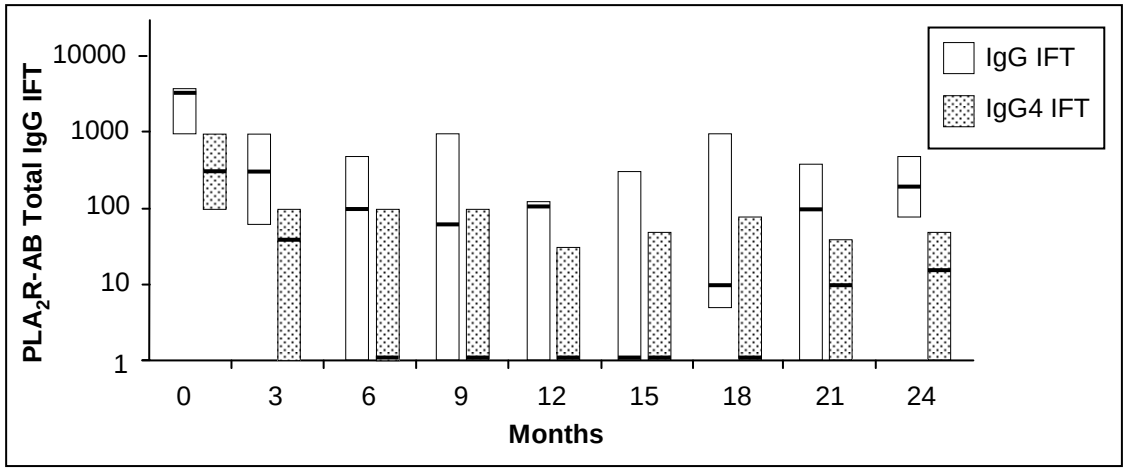
N (Prot)	51	37	26	19	15	13	11	4	4
N (Alb)	49	34	21	19	11	10	4	4	2

Bi



N (IgG-ELISA)	51	42	27	22	17	12	6	5	4
N (IgG4-ELISA)	51	42	27	22	17	12	6	5	4

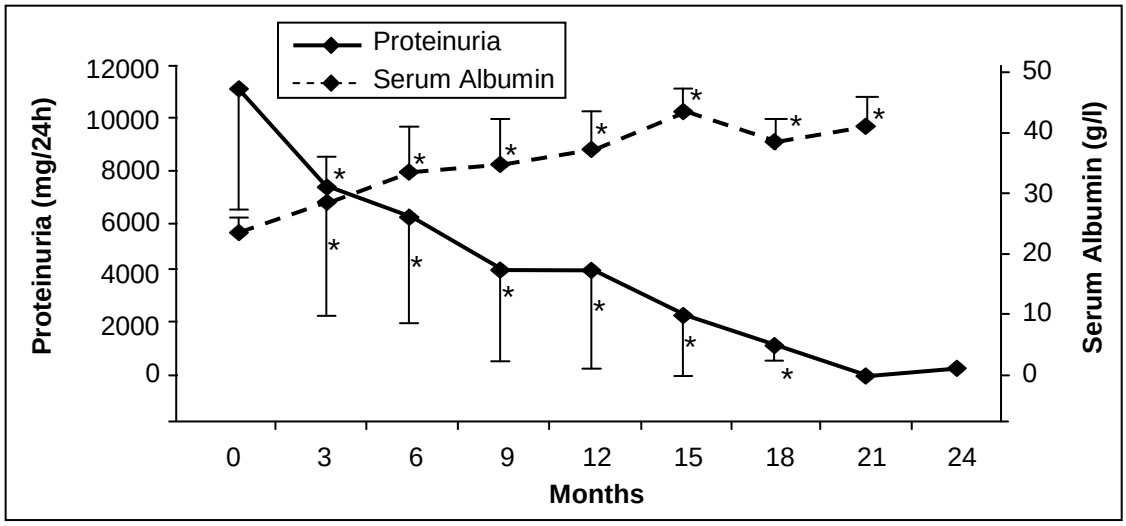
Ci



N (IgG-IFT)	53	43	28	22	17	13	7	5	4
N (IgG4-IFT)	51	42	27	22	17	12	7	5	4

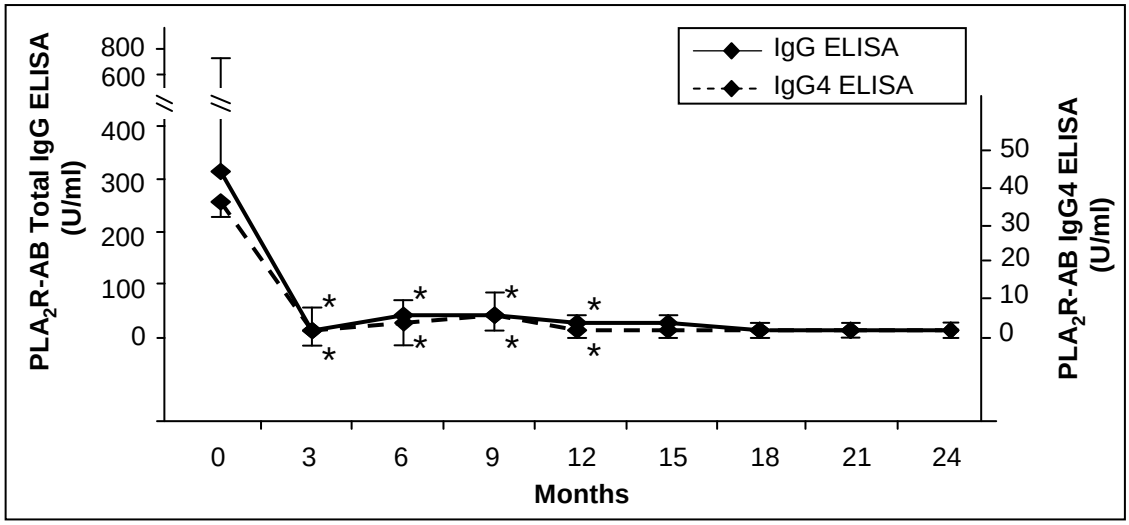
Supplemental Figure 2

Aii



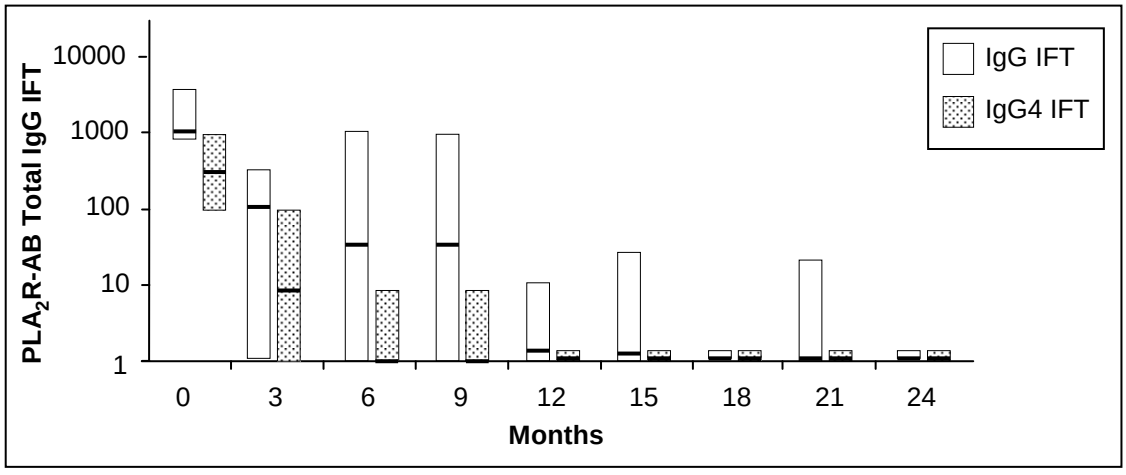
N (Prot)	32	26	20	14	9	8	3	1	1
N (Alb)	31	21	20	16	9	7	3	2	0

Bii



N (IgG-ELISA)	32	31	24	21	14	8	5	3	2
N (IgG4-ELISA)	32	31	24	21	14	8	5	3	2

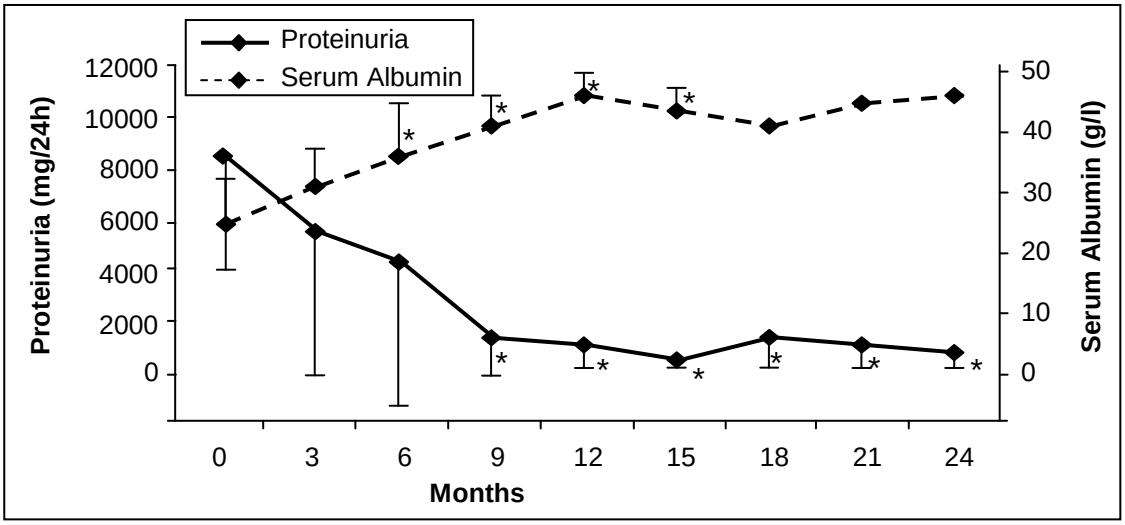
Cii



N (IgG-IFT)	32	31	24	21	14	8	5	3	2
N (IgG4-IFT)	32	30	24	21	14	8	5	3	2

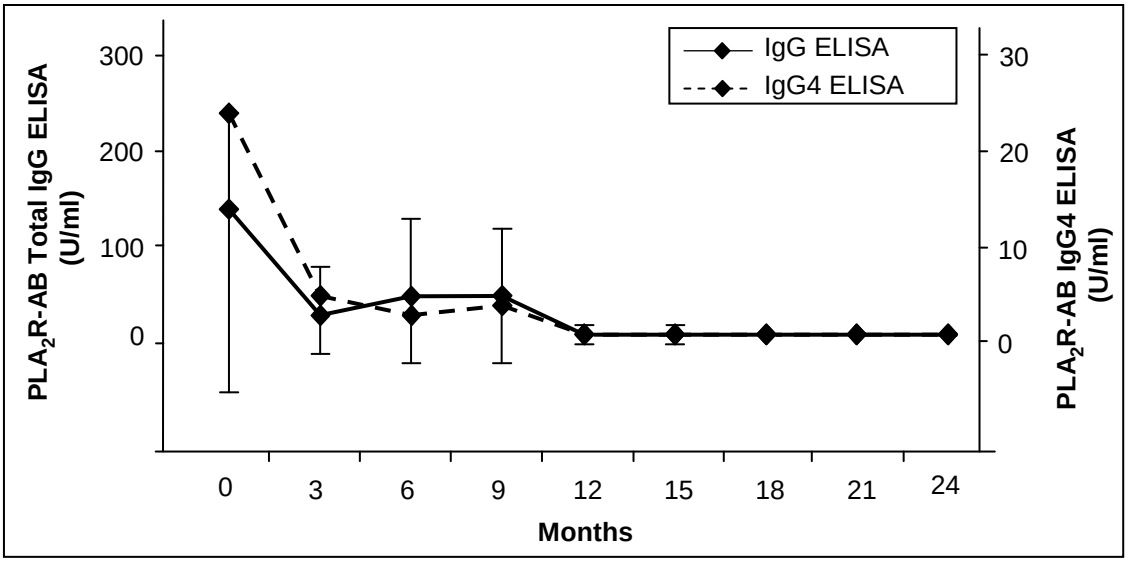
Supplemental Figure 2

Aiii



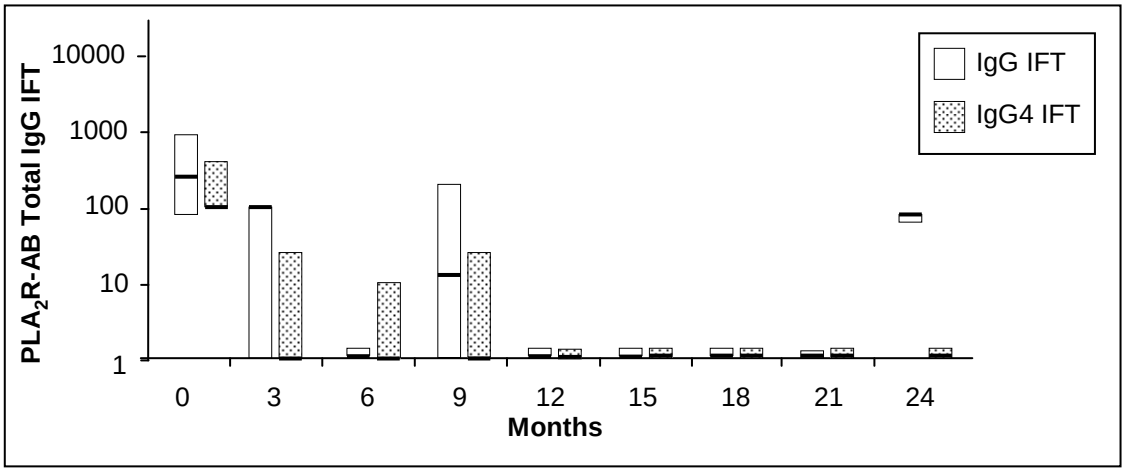
N (Prot)	9	8	5	4	4	2	2	2	2
N (Alb)	9	7	5	4	3	2	1	1	1

Biii



N (IgG-ELISA)	9	7	5	4	4	2	1	1	1
N (IgG4-ELISA)	9	7	5	4	4	2	1	1	1

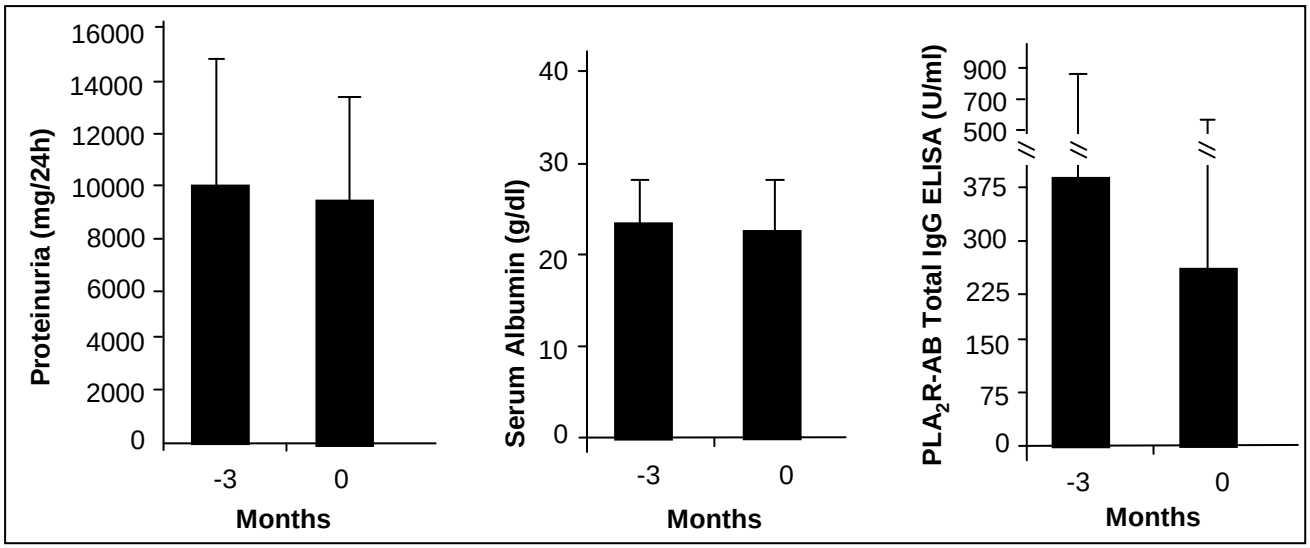
Ciii



N (IgG-IFT)	9	7	5	4	4	2	1	1	1
N (IgG4-IFT)	9	7	5	4	4	2	1	1	1

Supplemental Figure 3

A



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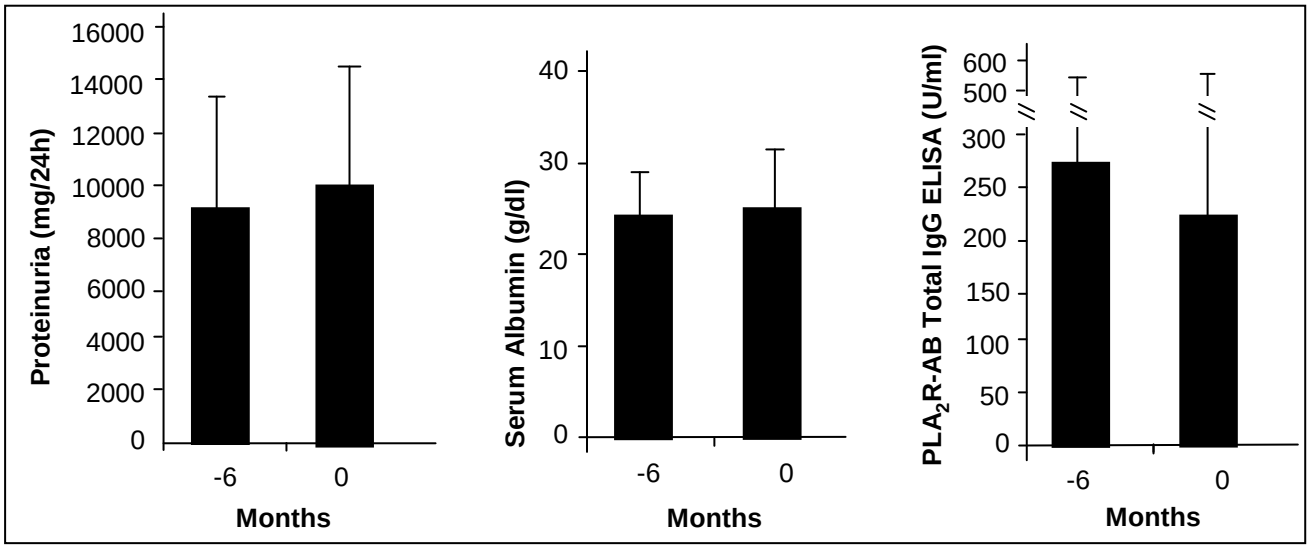

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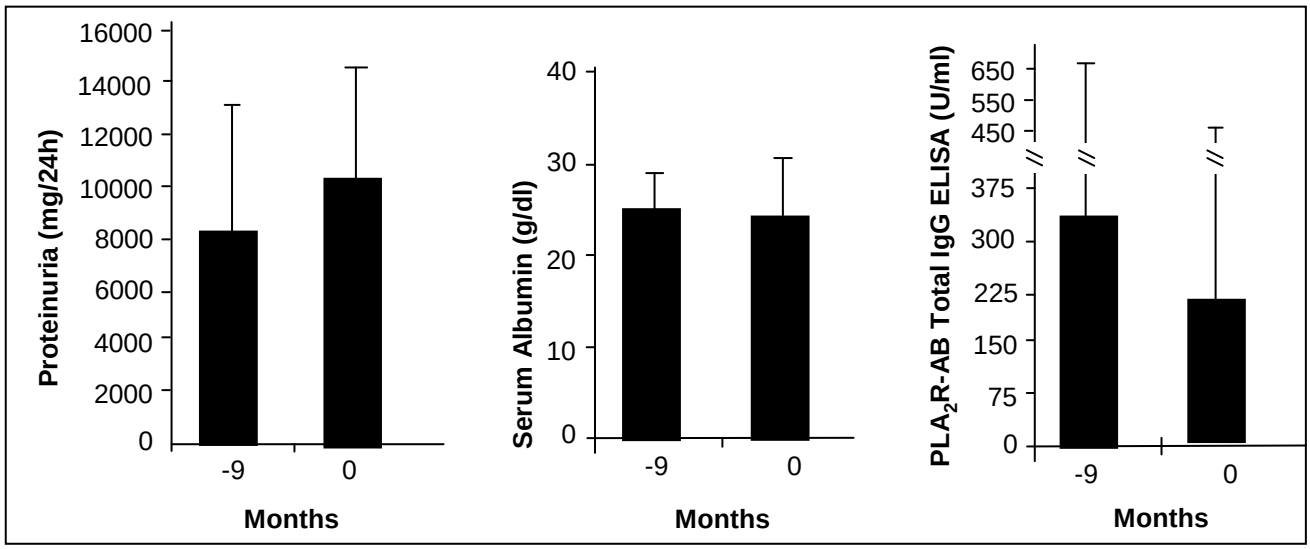
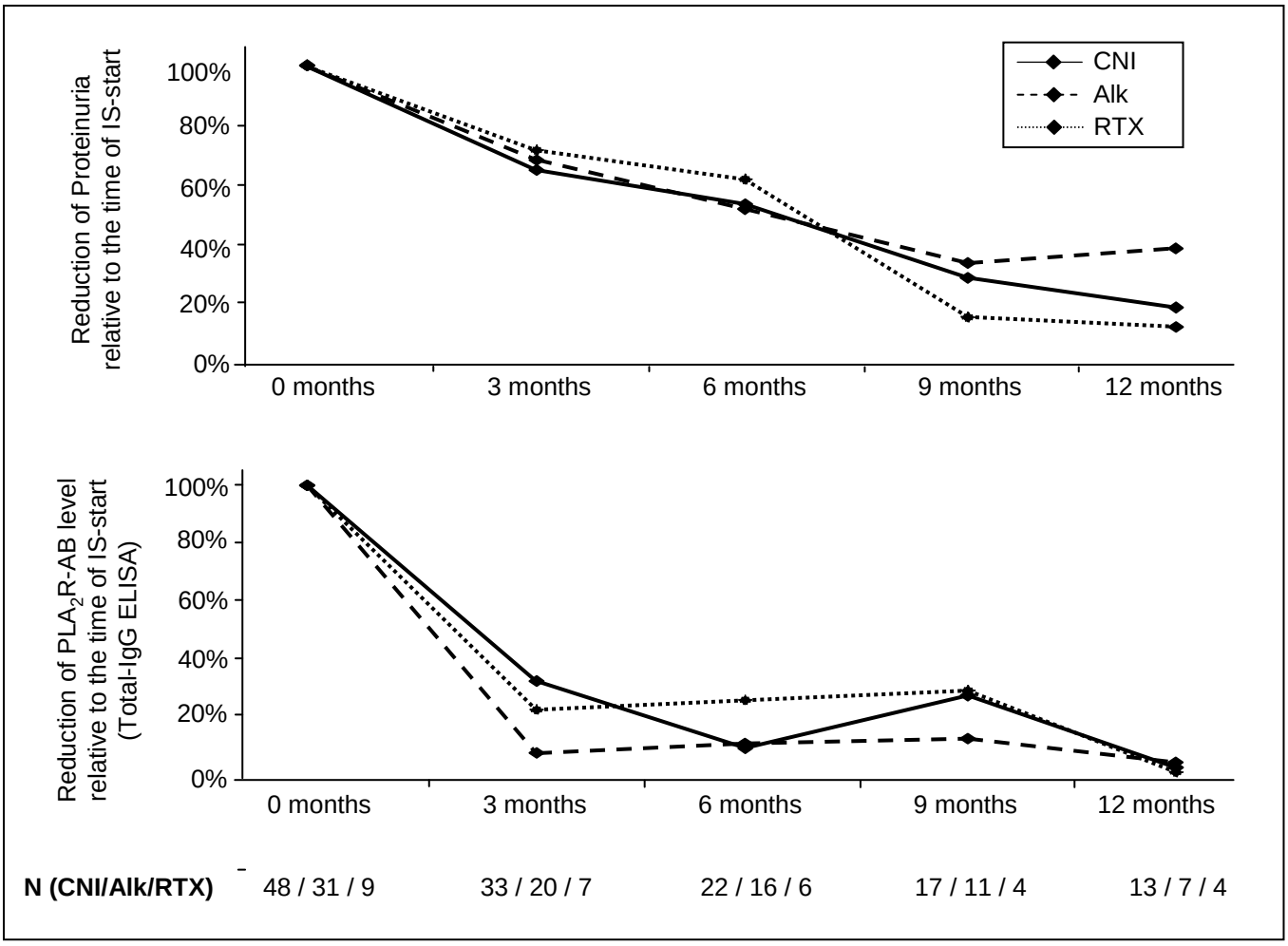
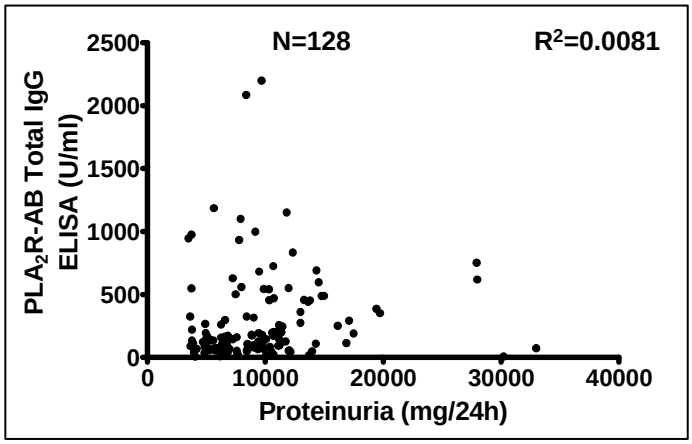
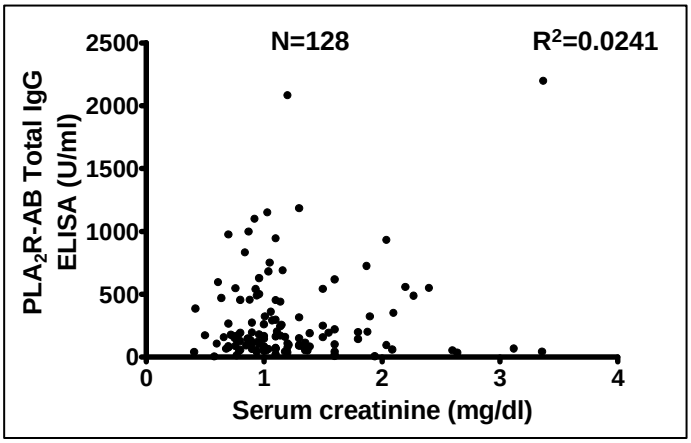


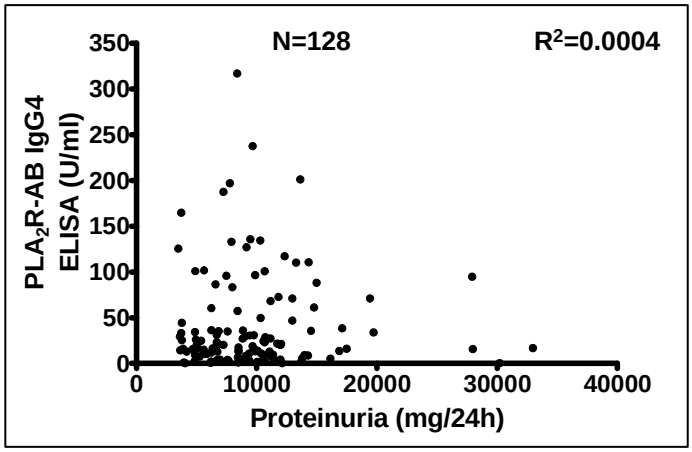
Supplemental Figure 4

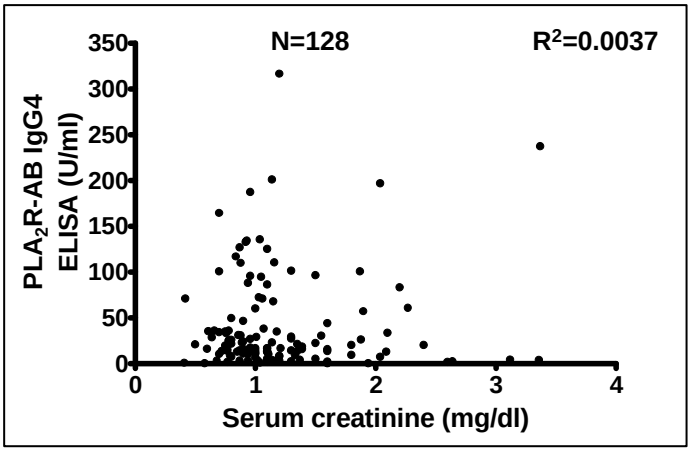


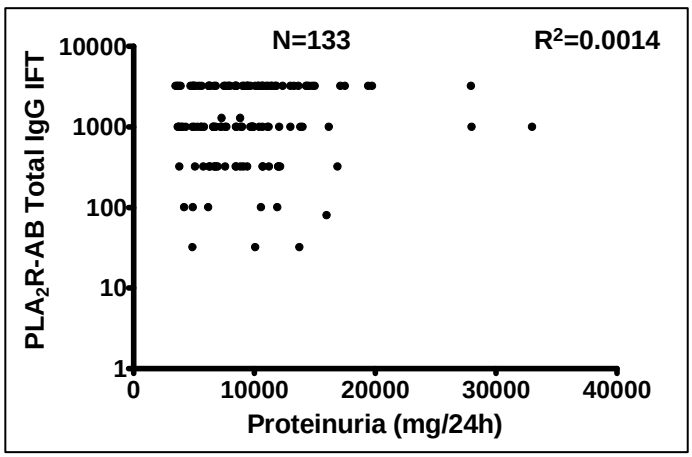
Supplemental Figure 5

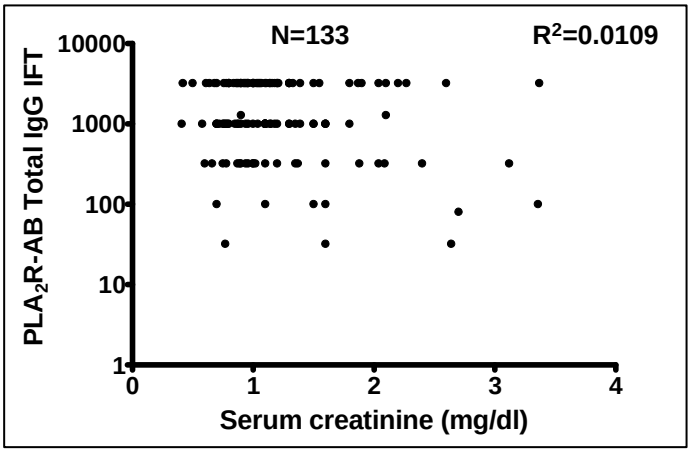


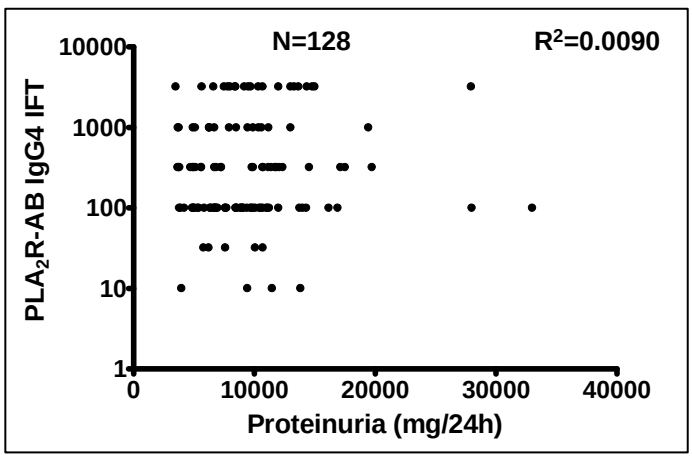


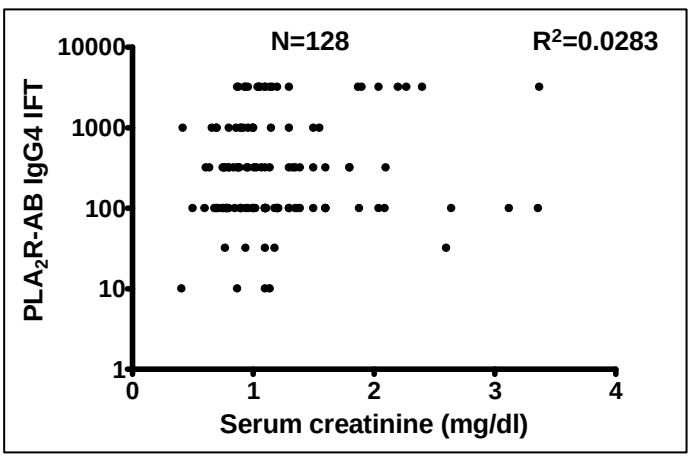




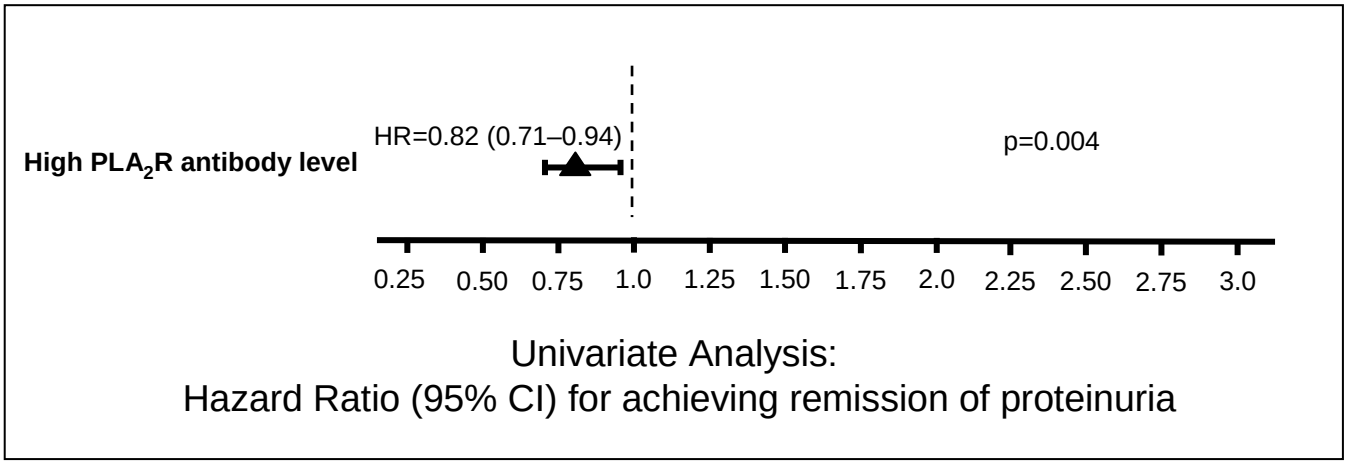






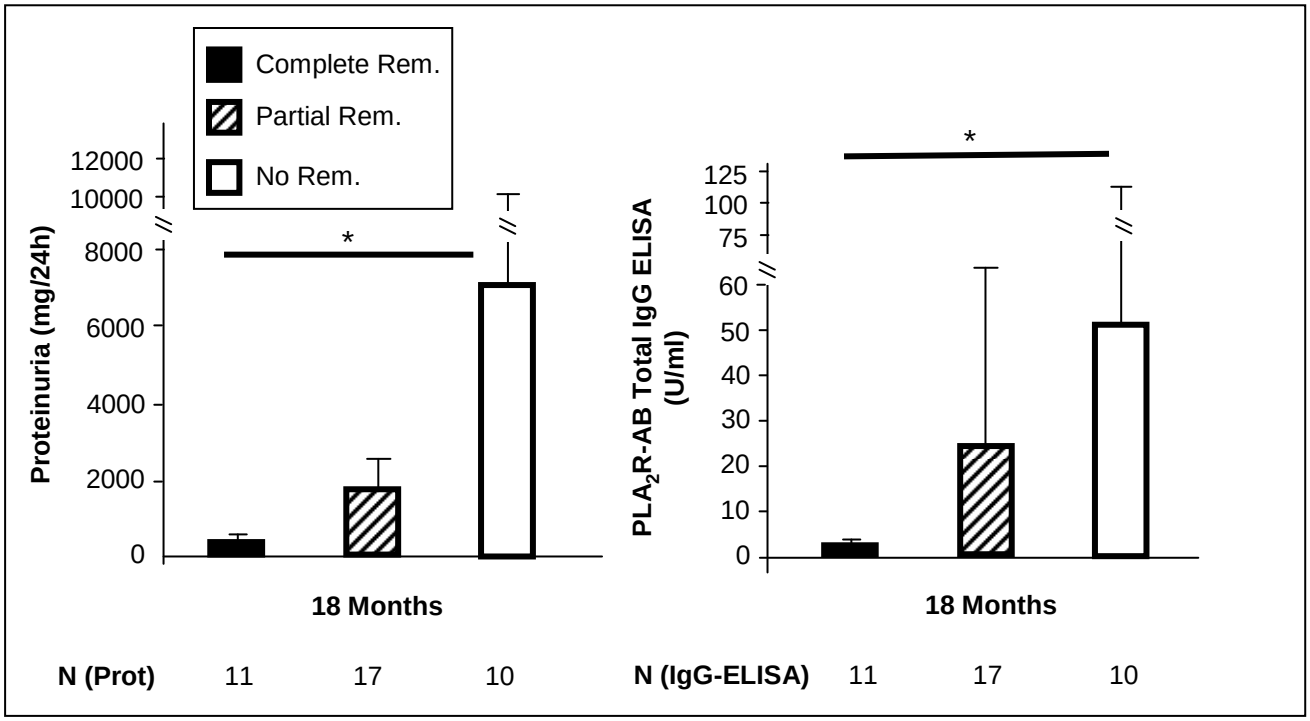


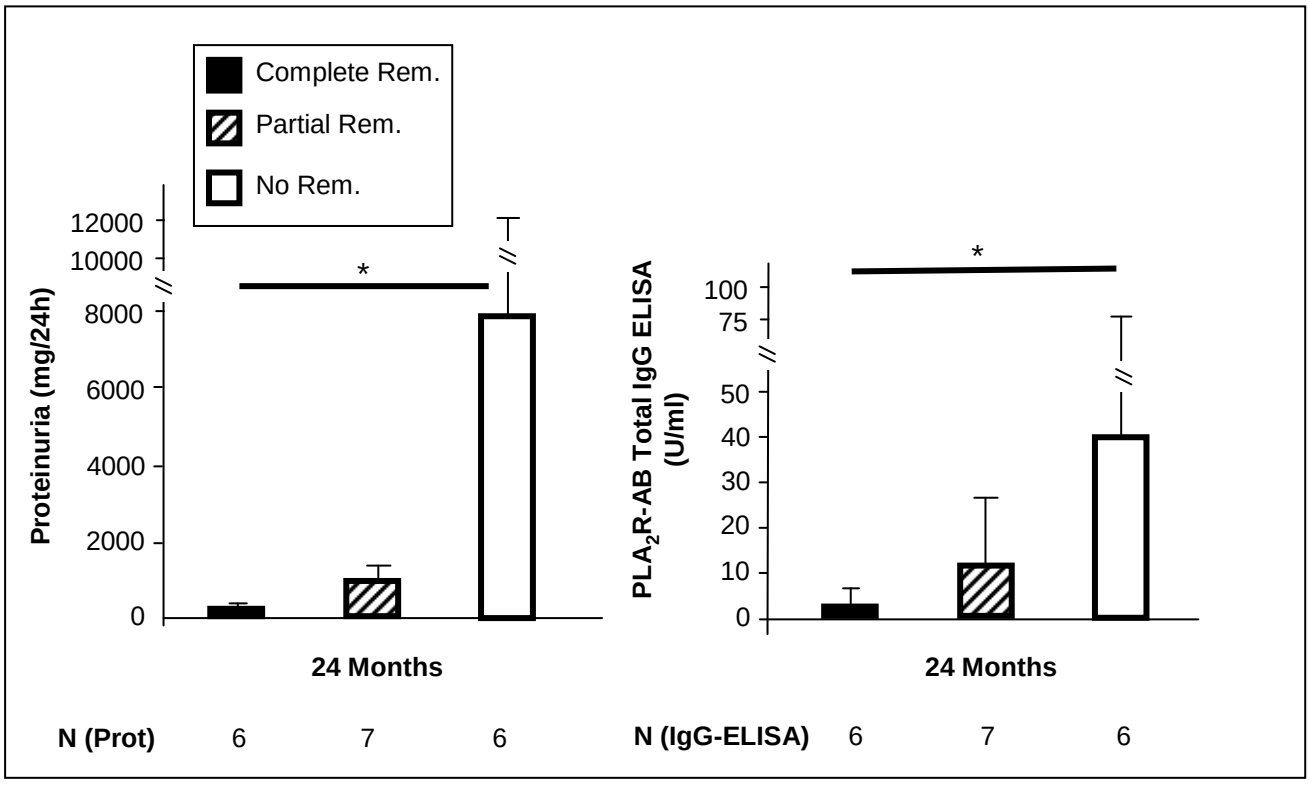
Supplemental Figure 6



Univariate Analysis:
Hazard Ratio (95% CI) for achieving remission of proteinuria

Supplemental Figure 7





Supplemental Table 1

Whole study population (Fig. 2)	**PLA_2R-AB Total IgG ELISA (U/ml)**		**PLA_2R-AB IgG4 ELISA (U/ml)**	
Time point (months)	**Median**	**25th – 75th percentile**	**Median**	**25th – 75th percentile**
0	147.5	73.2 – 351.0	18.9	9.1 – 44.5
3	49.5	11.4 – 158.4	4.8	1.1 – 20.2
6	34.8	6.6 – 106.7	2.4	0.2 – 10.9
9	18.8	3.5 – 54.7	1.0	0.0 – 6.5
12	7.0	2.7 – 28.4	0.2	0.0 – 2.5
15	6.3	2.8 – 36.6	0.2	0.0 – 3.5
18	4.2	2.6 – 28.3	0.1	0.0 – 2.8
21	11.6	2.7 – 18.5	0.5	0.0 – 1.8
24	10.2	2.8 – 19.8	0.1	0.0 – 2.0

Patients under immunosuppression (Fig. 3)	**PLA_2R-AB Total IgG ELISA (U/ml)**		**PLA_2R-AB IgG4 ELISA (U/ml)**	
Time point (months)	**Median**	**25th – 75th percentile**	**Median**	**25th – 75th percentile**
0	142.2	62.2 – 321.5	19.5	8.8 – 44.3
3	12.4	3.8 – 32.6	1.2	0.1 – 6.0
6	8.3	2.9 – 33.1	0.4	0.0 – 2.8
9	5.7	2.7 – 34.1	0.1	0.0 – 2.4
12	4.1	2.5 – 15.0	0.1	0.0 – 0.8
15	3.2	2.7 – 26.5	0.1	0.0 – 2.0
18	3.6	2.3 – 20.8	0.0	0.0 – 1.6
21	7.6	2.6 – 15.5	0.1	0.0 – 1.4
24	7.9	2.6 – 19.5	0.0	0.0 – 2.2

Supplemental Figure 1:

PLA_2R antibody levels measured by IFT

Figure 1A): Total IgG PLA_2R antibody levels and IgG4 PLA_2R antibody levels of all patients included in the study:

PLA_2R antibody levels fell over the time of follow-up. There was no difference between the change of total IgG and IgG4 subclass PLA_2R antibody levels. Boxes represent median (line) and 25^{th} and 75^{th} percentiles. The IgG4 PLA_2R subclass antibody levels are lower than total IgG PLA_2R antibody levels. Time 0 shows data at the time of the first PLA_2R antibody measurement. “N” gives the number of patients where data were available at the different time points.

Figure 1B: Total IgG PLA_2R antibody levels and IgG4 PLA_2R subclass antibody levels of patients with immunosuppressive therapy:

The absolute IgG4 PLA_2R antibody levels are lower than the total IgG PLA_2R antibody levels, yet the changes of total IgG PLA_2R antibody levels were not different to the changes of IgG4 PLA_2R antibody levels. Boxes represent median (line) and 25^{th} and 75^{th} percentiles. Time “0” shows data at the time of the start of immunosuppression. “N” gives the number of patients where data were available at the different time points.

Figure 1C: PLA_2R antibody levels in 12 patients with spontaneous remission or no remission of proteinuria after 15 months.

At the time of the inclusion in the study PLA_2R antibody levels (both total IgG and IgG4 subclass) were not different between the patients who experienced remission and those who did not show significant improvement of proteinuria after 15 months. In those patients with remission of proteinuria antibody levels fell during the follow-up and after 15 months were lower when compared to the time of inclusion in the study and to the patients who did not show remission of proteinuria.

Time “0” shows data at the time of the first PLA_2R measurement. “N” gives the number of patients where data were available at the different time points.

Supplemental Figure 2:

Proteinuria (A), serum albumin (B) and PLA_2R antibody levels (C) of patients treated with different immunosuppressive medications.

Patients were treated with calcineurin inhibitors (Ai, Bi, Ci), alkylating agents (Aii, Bii, Cii) or rituximab (Aiii, Biii, Ciii).

When patients who received calcineurin inhibitors (i) were compared with patients who received alkylating agents (ii) or Rituximab (iii) there were no differences in the degree of proteinuria or the serum albumin levels (Ai, Aii, Aiii) at the start of the immunosuppressive therapy (0 Months). There were also no differences between the three groups in their antibody levels (Bi-iii, Ci-iii).

There are minor differences in the late time points between PLA_2R antibody levels measured by IFT and ELISA. Fig Ci shows increasing titers by IFT, especially at the 24 month time point, whereas there is no significant change in Fig Bi. A similar pattern occurs in the single patient at the 24 month time point in Fig Ciii vs. Fig Biii. These changes relate to elevated PLA_2R antibody titers measured by IFT in 5 patients. One patient had a relapse of proteinuria. 2 patients showed a further decrease of PLA_2R antibody titers in the follow up beyond 24 months and became negative. In 2 patients the follow up with the IFT was stopped after 24 months.

“N” gives the numbers of patients for whom data were available at the different time points. Follow-up of patients was stopped at the time when immunosuppressive treatment was switched from one agent to another.

“*” shows a statistical significant difference between the time point and the start of immunosuppression.

Supplemental Figure 3:

Proteinuria, serum albumin and PLA_2R antibody levels 9 months, 6 months and 3 months before start of immunosuppressive treatment.

42 patients were treated for at least 3 months with supportive treatment before start of immunosuppression (A). In 23 patients supportive treatment was performed for at least 6 months (B), and in 8 patients for at least 9 months (C) before immunosuppression was started. Changes of proteinuria, serum albumin and PLA_2R antibody levels in all three groups were not statistically significant.

Supplemental Figure 4

Changes in PLA_2R antibody levels and proteinuria in all patients, following immunosuppressive therapy with all three treatment protocols (calcineurin inhibitors, alkylating agents, rituximab).

Data are presented as the relation of PLA_2R antibody levels or proteinuria at the given time point (3, 6, 9 or 12 months) to the time of start of immunosuppression (Time 0). Data are presented for all patients treated with calcineurin inhibitors, alkylating agents or rituximab, for whom both PLA_2R antibody levels and proteinuria for the given time points were available. Follow-up of patients was stopped at the time when immunosuppressive treatment was switched from one agent to another. There was no significant difference in the decrease of PLA_2R antibody levels and in the decrease of proteinuria between the three treatment groups. The decrease of PLA_2R antibody levels was more rapid and followed by the decrease in proteinuria.

Supplemental Figure 5:

There is no correlation between proteinuria or serum creatinine and total IgG or IgG4 PLA_2R antibody levels at the time of the inclusion in the study.

"N" gives the number of patients for whom data were available for the given time point.

Supplemental Figure 6:

Univariate Cox regression analysis

Total IgG PLA_2R antibody levels measured by ELISA were identified as risk factors for not achieving a remission of proteinuria in the 128 patients for whom ELISA PLA_2R antibody levels at study start were available. Hazard Ratio for achieving a remission of proteinuria is expressed per ln-unit (natural logarithm) of PLA_2R antibody levels measured by ELISA.

Supplemental Figure 7:

Proteinuria and PLA_2R antibody levels (Total IgG ELISA) of patients with complete, partial or no remission of proteinuria after 18 months (A) and 24 months (B).

At 18 months data on proteinuria was available in 44 patients. In 38 of these patients data on PLA_2R antibody levels were available. Patients with no remission of proteinuria (N=10) have statistically significant higher PLA_2R antibody levels than patients with complete remission of proteinuria (N=11) (*shows $p<0.05$). Patients with complete remission of proteinuria have lower PLA_2R antibody levels than patients with partial remission of proteinuria (N=17), however, the differences in the PLA_2R antibody levels between patients reaching complete or partial remission of proteinuria do not reach statistical significance.

At 24 months data on proteinuria was available in 22 patients. In 19 of these patients data on PLA_2R antibody levels were available. Patients with no remission of proteinuria (N=6) have statistically significant higher PLA_2R antibody levels than patients with complete remission of proteinuria (N=6) (*shows $p<0.05$). Patients with complete remission of proteinuria have lower PLA_2R antibody levels than patients with partial remission of proteinuria (N=7), however, the differences in the PLA_2R antibody levels between patients reaching complete or partial remission of proteinuria do not reach statistical significance.

Supplemental Table 1:

Median values of PLA_2R antibody levels measured by ELISA, presented in figures 1 and 2.

Supplemental Methods:

When the quantification of PLA_2R antibody levels by IFT was conducted by serial dilution of sera until the IFT was negative higher mean levels ± SD were obtained (1877±7) compared to levels when performed according to the manufacturer's recommendation, which allows a serial dilution of the sera up to a dilution of 1:3200 (1091±4). Median values (25^{th} percentile; 75^{th} percentile) of PLA_2R antibody levels at study start measured by IFT were 1000 (1000; 10000) when the quantification was conducted by serial dilution of sera until the IFT was negative and 1000 (1000; 3200) when performed according to the manufacturer's recommendation.

Data presented here are obtained by dilutions done until 1:3200.