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SUPPLEMENTARY FIGURES

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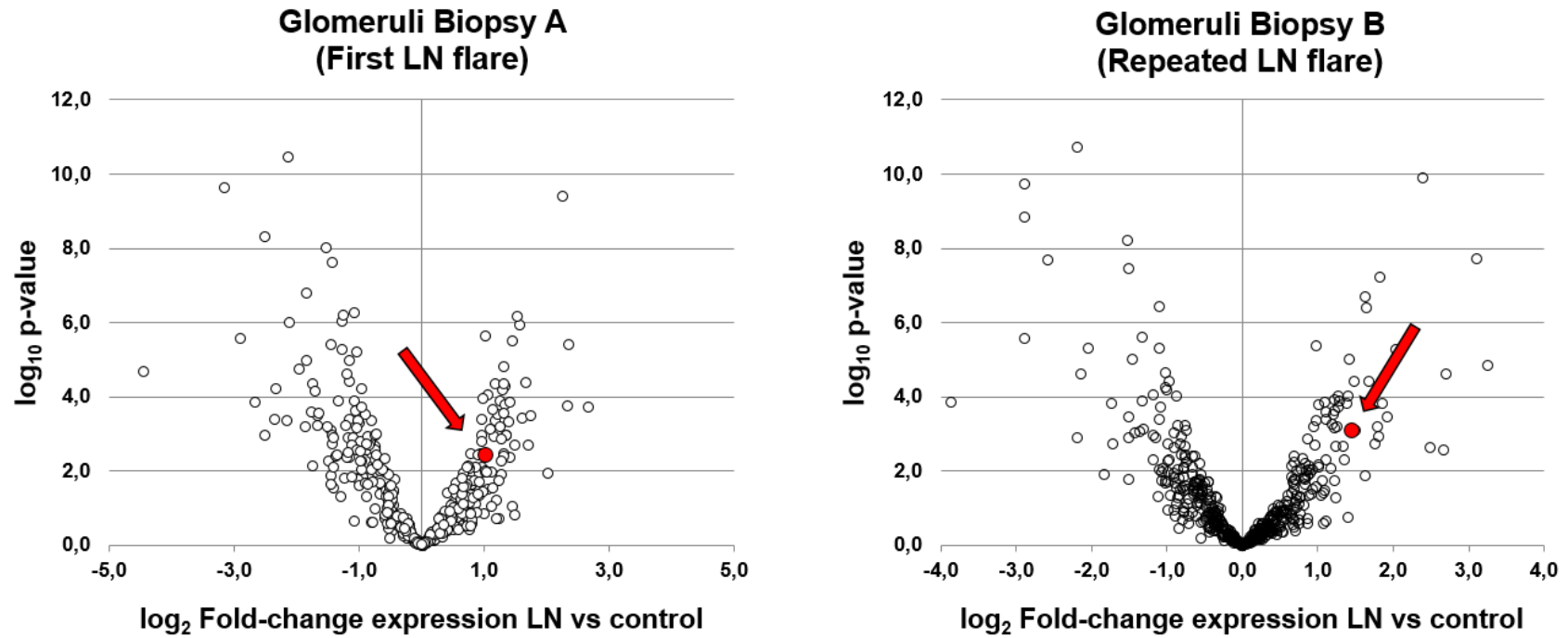
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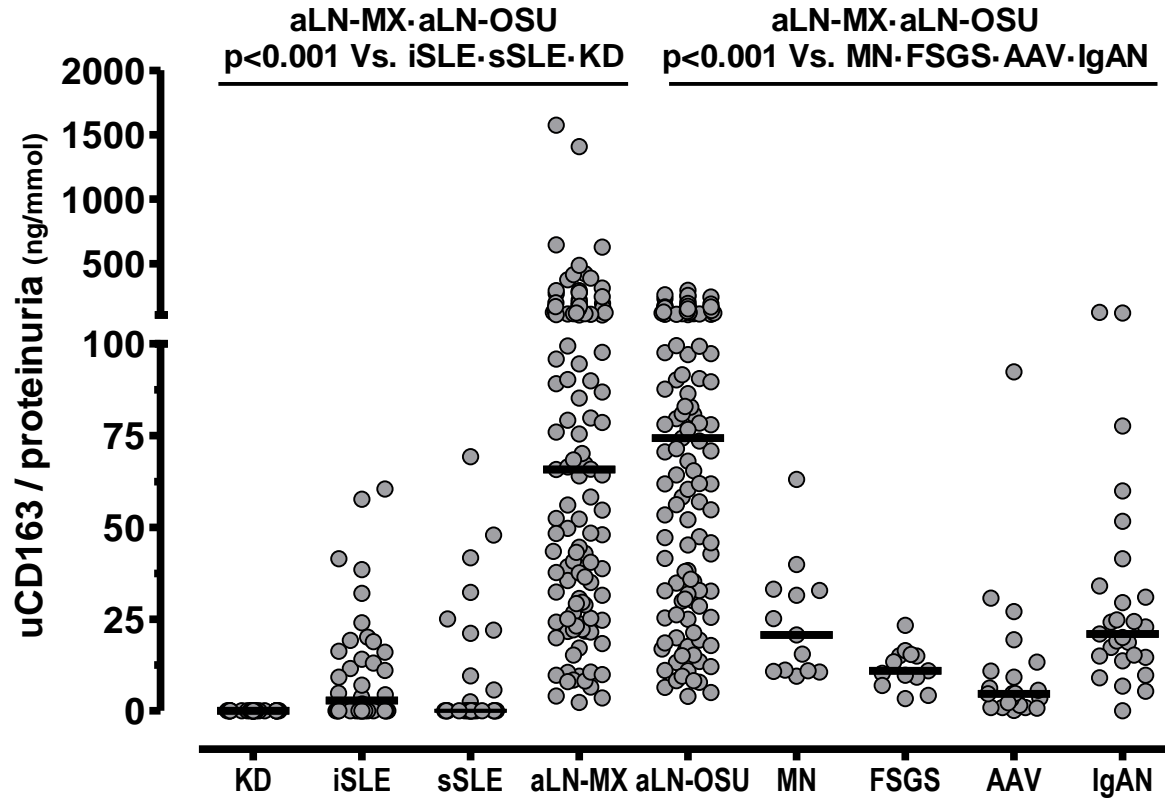
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Supplementary Figure 1. Volcano plots show that CD163 gene expression is higher in glomeruli from lupus nephritis patients compared to healthy controls the first presentation of LN and at LN flare



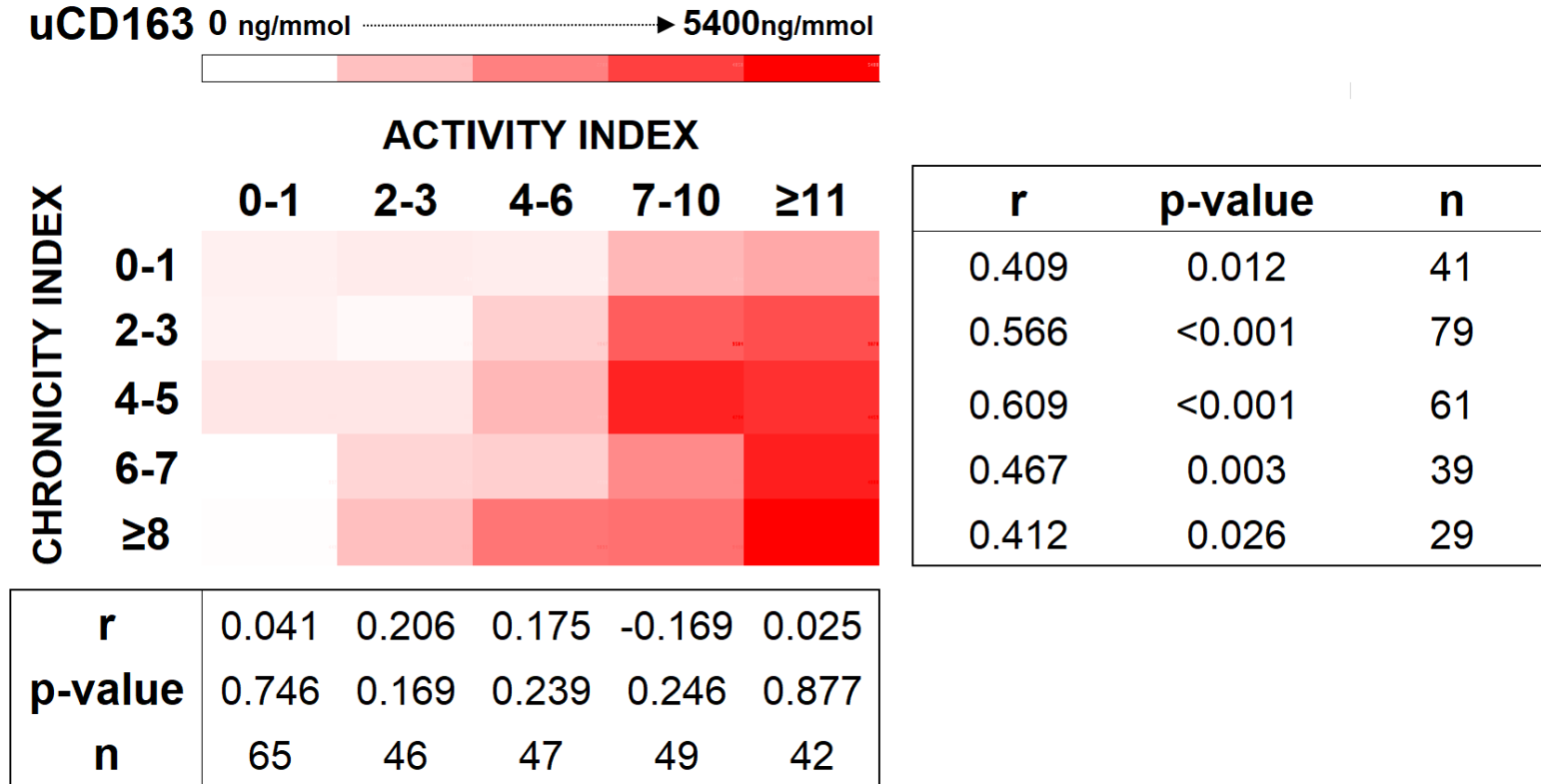
Volcano plots show that CD163 gene expression is higher in glomeruli from lupus nephritis patients compared to healthy controls the first presentation of LN and at LN flare. The arrow and dot represent CD163 gene expression. Information obtained from the authors previous study¹⁵.

Supplementary Figure 2. Urinary CD163 levels corrected by total proteinuria in different glomerular diseases.



Abbreviations. KD, Kidney donors (n=30); iSLE, inactive SLE (n=40); sSLE, active extra-renal SLE (n=30); aLN-MX, active lupus nephritis Mexican cohort (n=120); aLN-OSU, active lupus nephritis OSU cohort (n=129); MN, membranous nephropathy (n=13); FSGS, focal and segmental glomerulosclerosis (n=13); AAV, active ANCA-associated vasculitis (n=23); IgAN, IgA nephropathy (n=27).

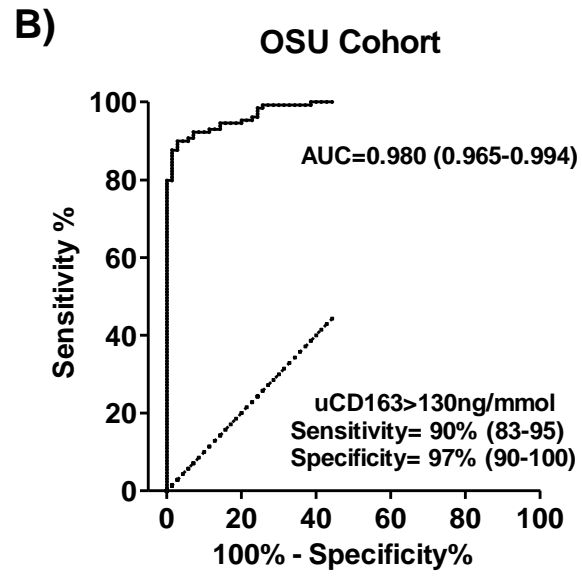
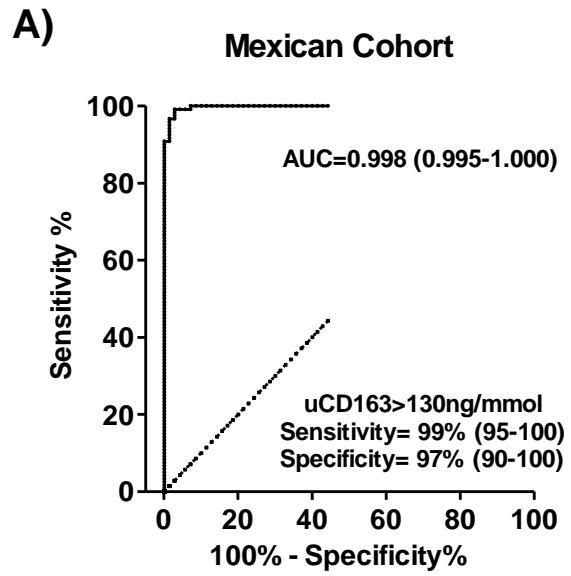
Supplementary Figure 3. Heatmap showing correlation (Spearman r) of uCD163 with histological activity and chronicity indices.



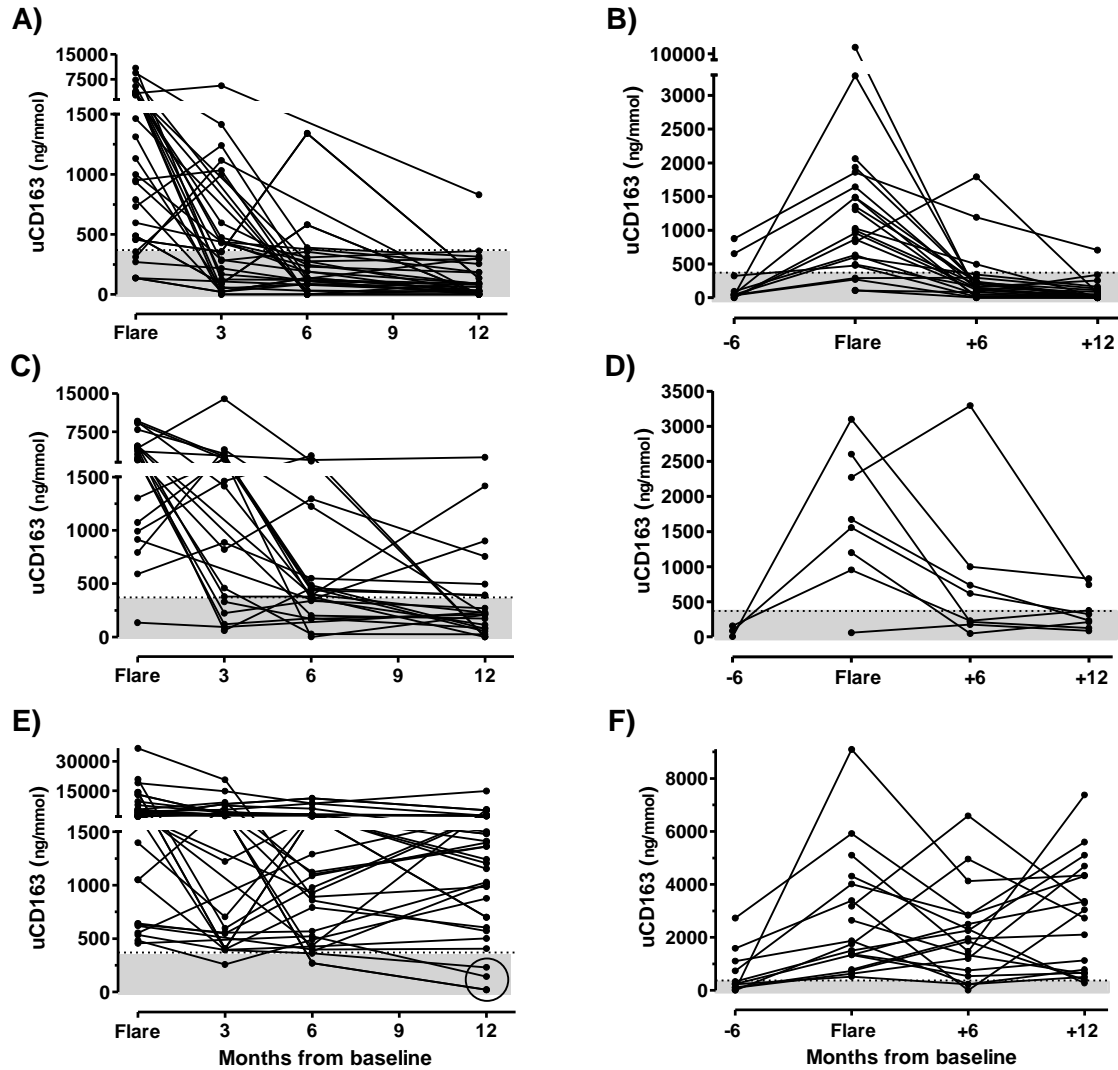
The right box shows the Spearman's coefficient between uCD163 and activity index at different levels of chronicity.

The lower box shows the Spearman's coefficient between uCD163 and chronicity index at different levels of activity.

Supplementary Figure 4. Diagnostic yield of uCD163 to differentiate between active and inactive lupus nephritis

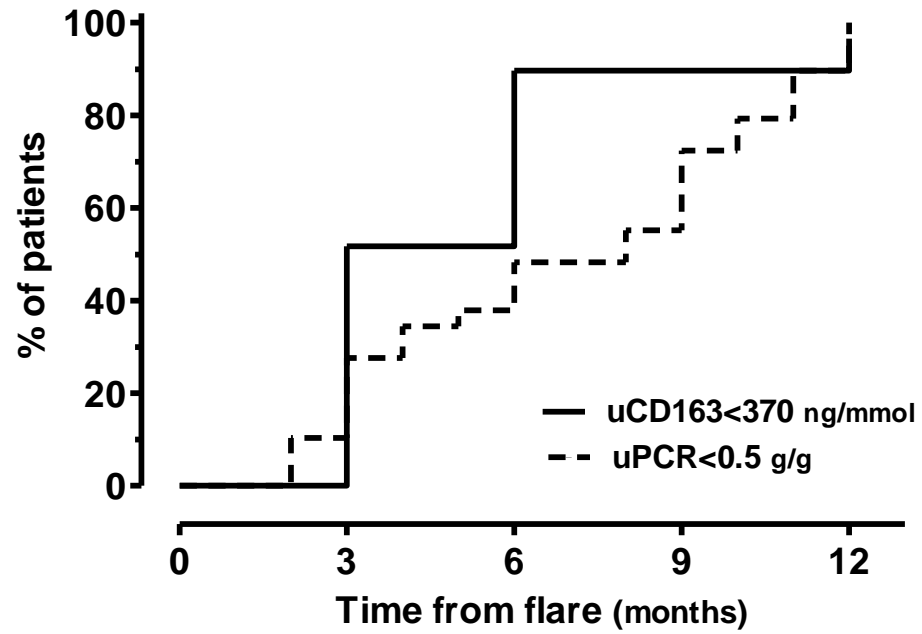


Supplementary Figure 5. Urinary CD163 levels over time in response to treatment

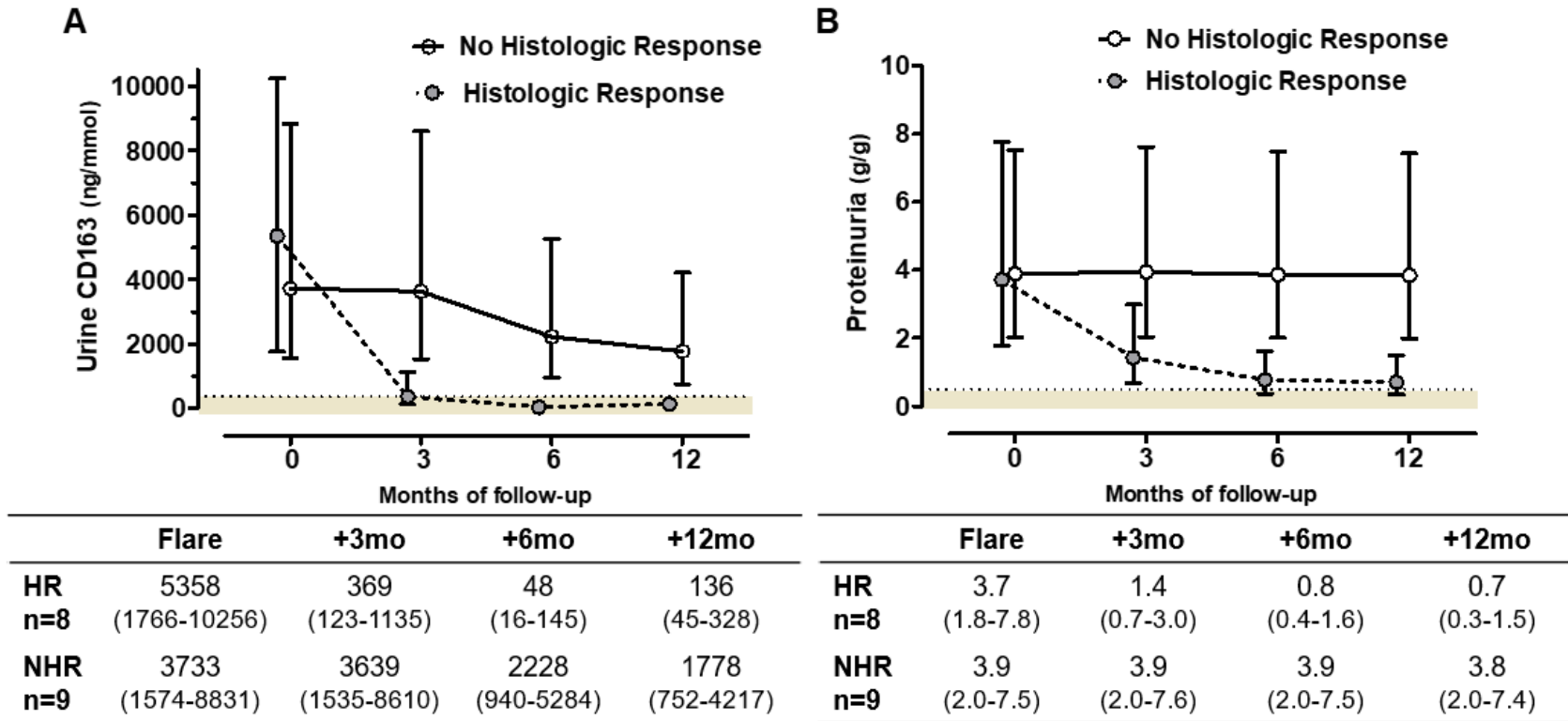


Patients are from the Mexican (A, C, E) and OSS (B, D, E) longitudinal cohorts. The time course of complete clinical renal responders is shown in A and B, partial clinical renal responders in C and D, and non-responders in E and F. The gray area represents uCD163 values below 370ng/mmol. The three encircled patients in Figure E progressed to end-stage renal disease before the 12th month.

Supplementary Figure 6. Time course of proteinuria and uCD163 by survival analysis.



Supplementary Figure 7. Urinary CD163 (A) and proteinuria (B) over time according to histological response



* The line and shaded in A represent the 370ng/mmol cutoff. The line and shaded area in B represent the 0.5g/g cutoff.

Abbreviations. HR, histological response (activity index \leq 1); NHR, no histological response (activity index $>$ 1).

Supplementary Table 1. Criteria for the clinical classification of severity of lupus nephritis flares.

Mild	Moderate	Severe
Increase in glomerular hematuria from <5 to >15 RBC/hpf and/or uPCR <1000mg/g	If baseline creatinine is: <2.0mg/dl, an increase of 0.3-1.0mg/dl >2.0mg/dl, an increase of 0.40-1.5mg/dl and/or If baseline uPCR is: <500mg/g, an increase to >1000mg/g 500-1000mg/g, an increase to >2000mg/g, but less than absolute increase of <5000mg/g >1000mg/g, an increase of >2-fold with absolute uPCR<5000mg/g	If baseline creatinine is: <2mg/dl, an increase of 1.0mg/dl >2mg/dl, an increase of >1.5mg/dl and/or An absolute increase of uPCR>5000mg/g

Abbreviations. RBC/hpf, red blood cells per high-power field; uPCR, 24h urine protein to creatinine ratio.

Supplementary Table 2. Characteristics of the patients included in the cross-sectional evaluation.

	Active LN Mexican cohort n=120	Active LN OSU cohort n=129	Inactive LN n=70	Healthy kidney donors n=31	PLA2R-MN n=13	FSGS n=13	Renal active AAV n=22	IgAN n=27
Age, years	32 (25-39)	31 (26-40)	42 (30-52)	34 (29-41)	42 (37-59)	37 (27-48)	55 (47-63)	45 (29-55)
Female, n (%)	108 (90)	106 (82)	64 (91)	23 (74)	6 (46)	5 (39)	16 (73)	10 (37)
Race, n (%)								
Caucasian	1 (1)	61 (47)	21 (30)	12 (39)	1 (8)	0 (0)	0 (0)	22 (82)
African American	0 (0)	56 (44)	11 (16)	5 (16)	0 (0)	0 (0)	0 (0)	3 (11)
Asian	0 (0)	4 (3)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (7)
Mexican-mestizo	119 (99)	0 (0)	38 (54)	10 (32)	12 (92)	13 (100)	22 (100)	0(0)
Other	0 (0)	8 (6)	0 (0)	4 (13)	0 (0)	0 (0)	0 (0)	0(0)
Creatinine, mg/dL	1.1 (0.7-2.0)	0.9 (0.7-1.6)	0.7 (0.6-0.9)	0.8 (0.7-0.9)	1.0 (0.9-1.3)	1.1 (0.9-1.6)	2.5 (1.1-3.5)	1.1 (1.0-1.8)
eGFR, mL/min/1.73m ²	68 (35-110)	90 (48-123)	103 (86-118)	101 (96-109)	76 (61-90)	89 (45-111)	26 (14-68)	66 (42-107)
Proteinuria, 24h-g/g	3.3 (2.2-5.2)	2.6 (0.9-4.8)	0.1 (0.1-0.2)	0.1 (0.0-0.1)	5.2 (2.4-8.3)	4.8 (1.6-10.1)	1.6 (0.5-3.2)	1.3 (0.7-2.0)
+ve dsDNA-Ab	101 (84)	89 (69)	0 (0)	-	0 (0)	0 (0)	0 (0)	0 (0)
C3, mg/dL	68 (44-88)	62 (43-86)	101 (87-118)	-	134 (95-140)	149 (122-174)	116 (97-128)	131 (112-150)
C4, mg/dL	8 (8-13)	11 (8-18)	20 (10-27)	-	31 (28-48)	39 (30-46)	30 (18-41)	29 (22-41)

* All values are expressed as median (interquartile range) or number (relative frequencies).

Abbreviations. LN, lupus nephritis; OSU, Ohio State University cohort; PLA2R-MN, phospholipase A2-receptor positive membranous nephropathy; FSGS, focal and segmental glomerulosclerosis; AAV, ANCA-associated vasculitis; IgAN, IgA nephropathy; eGFR, estimated glomerular filtration rate calculated by the CKD-EPI formula; dsDNA-Ab, double-strand DNA antibodies; C3, complement protein C3; C4, complement protein C4.

Supplementary Table 3. Histological characteristics of the patients included in the study.

	Active LN Mexican cohort n=120	Active LN OSU biopsy cohort n=129
ISN-RPS classification		
Class II	2 (2)	11 (9)
Class III ± V	35 (31)	38 (29)
Class IV ± V	67 (59)	62 (48)
Class V	9 (8)	18 (14)
ACTIVITY INDEX COMPONENTS		
Activity index	4 (1-9)	3 (2-6)
Fibrinoid necrosis		
<5%	82 (73)	82 (63)
6-25%	24 (21)	33 (26)
26-50%	5 (4)	6 (5)
>50%	2 (2)	8 (6)
Endocapillary hypercellularity		
<5%	51 (45)	28 (22)
6-25%	34 (31)	40 (31)
26-50%	14 (12)	32 (25)
>50%	14 (12)	29 (22)
Leukostasis		
<5%	55 (49)	67 (52)
6-25%	30 (26)	48 (37)
26-50%	18 (16)	13 (10)
>50%	10 (9)	1 (1)
Hyaline thrombi		
<5%	94 (83)	86 (66)
6-25%	13 (11)	28 (22)
26-50%	3 (3)	10 (8)
>50%	3 (3)	5 (4)
Wire loops		
<5%	80 (71)	83 (64)
6-25%	23 (21)	27 (21)
26-50%	5 (4)	12 (9)
>50%	5 (4)	7 (6)
Karyorrhexis		
<5%	89 (79)	82 (63)
6-25%	17 (15)	33 (26)
26-50%	6 (5)	6 (5)
>50%	1 (1)	8 (6)
Cellular crescents		
<5%	74 (65)	86 (66)
6-25%	26 (23)	28 (22)

26-50%	13 (12)	10 (8)
>50%	0 (0)	5 (4)
Interstitial inflammation		
<5%	12 (11)	39 (30)
6-25%	82 (72)	67 (52)
26-50%	15 (13)	23 (18)
>50%	4 (4)	0 (0)
CHRONICITY INDEX COMPONENTS		
Chronicity index	4 (3-6)	5 (2-8)
Total sclerosis		
<5%	18 (16)	57 (44)
6-25%	36 (32)	43 (33)
26-50%	29 (26)	22 (17)
>50%	30 (26)	7 (6)
Fibrous crescents		
<5%	75 (66)	92 (71)
6-25%	32 (28)	32 (25)
26-50%	5 (5)	5 (4)
>50%	1 (1)	0 (0)
Interstitial fibrosis		
<5%	3 (3)	31 (24)
6-25%	70 (62)	50 (39)
26-50%	29 (25)	40 (31)
>50%	11 (10)	8 (6)
Tubular atrophy		
<5%	8 (7)	30 (23)
6-25%	67 (59)	53 (41)
26-50%	25 (22)	38 (30)
>50%	13 (12)	8 (6)

Abbreviations. ISN-RPS, International Society of Nephrology-Renal Pathology Society classification.

Supplementary Table 4. Factors associated with the histologic activity index determined by linear regression analysis.

	Adjusted β	β	95% CI	p-value
Model 1: $r^2=0.304$				
Age	-0.183	-2.029	-3.62 to -0.44	0.002
Log ₁₀ eGFR	-0.186	-2.537	-4.2 to -0.95	0.002
Log ₁₀ proteinuria	0.219	2.576	1.20 to 3.89	<0.001
Log ₁₀ C3	-0.328	-6.921	-9.55 to -4.52	<0.001
Model 2: $r^2=0.359$				
Age	-0.170	-0.072	-0.12 to -0.03	0.003
Log ₁₀ eGFR	-0.148	-2.049	-3.62 to -0.48	0.011
Log ₁₀ C3	-0.259	-5.550	-8.04 to -3.06	<0.001
Log ₁₀ uCD163	0.343	2.858	1.88 to 3.84	<0.001
Model 3: $r^2=0.360$				
Age	-0.165	-5.632	-9.46 to -1.80	0.004
Log ₁₀ eGFR	-0.150	-2.065	-3.6 to -0.49	0.010
Log ₁₀ proteinuria	0.042	0.487	-1.12 to 2.09	0.550
Log ₁₀ C3	-0.262	-5.673	-8.17 to -3.18	<0.001
Log ₁₀ uCD163	0.343	2.647	1.53 to 3.77	<0.001

Abbreviations: eGFR, estimated glomerular filtration rate at baseline; C3, complement protein C3; uCD163, urinary CD163 levels.

Supplementary Table 5. Characteristics of the lupus nephritis flares included in the longitudinal evaluation.

	OSS cohort n=49	Mexican cohort n=82
Demographics and Laboratory		
Age, years	32 (26-39)	34 (25-40)
Female, n (%)	49 (100)	76 (93)
Race		
Caucasian	26 (53)	0 (0)
African American	18 (37)	0 (0)
Asian	4 (8)	0 (0)
Mexican Mestizo	0 (0)	82 (100)
Other	1 (2)	0 (0)
Creatinine, mg/dL	1.0 (0.8-1.4)	1.1 (0.7-2.2)
Estimated GFR, mL/min/1.73m ²	73 (51-102)	67 (26-110)
Proteinuria, g/g	3.3 (2.0-4.6)	3.3 (2.2-5.5)
Positive anti-dsDNA antibodies	39 (80)	31 (84)
Complement C3, mg/dL	71 (62-85)	61 (43-88)
Complement C4, mg/dL	13 (8-17)	8 (8-13)
SLEDAI-2k score, points	20 (15-27)	18 (14-22)
Histopathology		
ISN/RPS classification		
Class III ± V	9 (18)	28 (34)
Class IV ± V	33 (67)	47 (57)
Class V	7 (14)	7 (9)
Activity index	NA	4 (1-8)
Chronicity index	NA	4 (3-5)
Treatment and response to treatment*		
Induction to remission therapy		
Cyclophosphamide	5 (10)	23 (28)
Mycophenolate mofetil	32 (65)	53 (65)
Azathioprine	12 (25)	3 (4)
CNI + Mycophenolate	0 (0)	3 (4)
Response at 6 months		
Complete response	13 (27)	12 (15)
Partial response	12 (24)	29 (35)
No response	24 (49)	41 (50)
Response at 12 months		
Complete response	22 (45)	29 (35)
Partial response	9 (18)	22 (27)
No response	18 (37)	31 (38)

* All induction to remission schemes included oral corticosteroids.

Abbreviations. OSS, Ohio SLE Study cohort; dsDNA, double-strand DNA; CNI, calcineurin inhibitor; NA, not available.

Supplementary Table 6. Predictors of a 12-month complete clinical renal response

	Best cutoff	Sensitivity	Specificity
uCD163 at 6 months	<370 ng/mmol	0.90	0.87
Proteinuria at 6 months	<1.50 g/g	0.86	0.81
Anti-dsDNA Ab titer at 6 months	<57 UI/mL	0.62	0.48
Complement C3 at 6 months	>77 mg/dL	0.86	0.45
Complement C4 at 6 months	>22 mg/dL	0.21	0.68

Supplementary Table 7. Agreement tables between histological activity and clinical parameters in patients with repeated biopsies*

	Histologic Activity ≤ 1	Histologic Activity > 1	Agreement (kappa)
uCD163			
uCD163 < 370 ng/mmol	8	0	1.000
uCD163 > 370 ng/mmol	0	10	
Proteinuria			
Proteinuria < 0.5 g/g	4	0	0.526
Proteinuria > 0.5 g/g	4	10	
Proteinuria < 1.0 g/g	5	1	0.553
Proteinuria > 1.0 g/g	3	9	
Proteinuria < 1.5 g/g	5	1	0.553
Proteinuria > 1.5 g/g	3	9	
dsDNA			
Anti-dsDNA antibody negative	4	0	0.526
Anti-dsDNA antibody positive	4	10	
C3			
C3 within reference range	7	3	0.561
Low C3	1	7	
C4			
C4 within reference range	6	1	0.658
Low C4	2	9	

* 1 patient had class V LN on repeat biopsy; activity index does not apply to class V

Supplementary Table 8. Univariate Cox-regression analysis for doubling of serum creatinine over follow-up.

	Hazard Ratio	95% CI	p-value
Age, per year	0.95	0.91-0.99	0.039
Male gender, Vs. female	2.26	0.53-9.73	0.272
Race			
Caucasian	1.00	Reference	Reference
Mexican mestizo	9.09	1.06-78.0	0.044
African American	5.18	0.53-50.2	0.156
Baseline laboratories			
eGFR, per 10ml/min/1.73m ²	0.84	0.75-0.94	0.002
Proteinuria, per g/g	1.06	0.94-1.19	0.365
Hematuria, Vs. not	1.83	0.53-6.41	0.342
Hemoglobin, per g/dL	0.89	0.74-1.08	0.241
Albumin, per g/dL	1.21	0.68-2.15	0.511
Positive dsDNA-antibodies, Vs. not	1.52	0.61-3.80	0.375
Complement C3, per mg/dL	1.00	0.99-1.02	0.538
Complement C4, per mg/dL	1.01	0.96-1.06	0.662
Plasma CD163, per 100ng/mL	1.05	0.86-1.27	0.649
Urine CD163, per µg/mmol	1.05	0.99-1.12	0.083
Histologic parameters			
Activity index, per point	1.04	0.95-1.14	0.394
Chronicity index, per point	1.42	1.20-1.66	<0.001
Follow-up laboratories			
6-month			
eGFR, per 10ml/min/1.73m ²	0.65	0.56-0.76	<0.001
Proteinuria, per g/g	1.15	1.03-1.28	0.013
uCD163, per µg/mmol	1.19	1.02-1.39	0.031
12-month			
eGFR, per 10ml/min/1.73m ²	0.63	0.53-0.73	<0.001
Proteinuria, per g/g	1.31	1.15-1.50	<0.001
uCD163, per µg/mmol	1.27	1.12-1.44	<0.001
Punctual follow-up parameters			
6-month			
uCD163>370ng/mmol	2.82	1.11-7.16	0.029
Proteinuria>0.5g/g	5.65	0.76-42.2	0.092
12-month			
uCD163<370ng/mmol	3.62	1.43-9.20	0.007
Proteinuria>0.5g/g	7.82	1.73-33.4	0.005
12-month response to treatment			
Complete response	0.09	0.02-0.41	0.002
Partial response	0.40	0.15-1.09	0.073
No response	1.00	Reference	Reference

