Legend of supplemental material

Supplementary table 1: Components of activity and chronicity indices at 1st and 2nd kidney biopsy in all patients and in those who received a 2nd kidney biopsy for proteinuric flare, nephritic flare or protocol biopsy.
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Supplementary table 1: Components of activity and chronicity indices at 1st and 2nd kidney biopsy in all patients and in those who received a 2nd kidney biopsy for proteinuric flare, nephritic flare or protocol biopsy.

Variables	Overall pts (n=61)		Proteinuric flare (n=22)		Nephritic flare (n=25)		Protocol biopsy (n=14)	
Activity index								
Endocap. Hypercell, >0	58 (95%)	38 (62%)	20 (91%)	13 (59%)	24 (96%)	20 (80%)	14 (100%)	5 (36%)
Neutr infiltr/karyor, >0	52 (85%)	34 (56%)	16 (73%)	12 (54.5%)	23 (92%)	20 (80%)	13 (93%)	2 (14%)
Hyaline deposits, >0	50 (83%)°	24 (39%)	18 (82%)	9 (41%)	21 (84%)	15 (60%)	11 (85%)°	-
Cell/fibrocell cresc, >0	37 (62%)°	21 (34%)	11 (53%)°	6 (27%)	17 (68%)	13 (52%)	9 (64%)	2 (14%)
Fibr necr >0	29 (47.5%)	16 (26%)	10 (45.5%)	5 (23%)	13 (52%)	10 (40%)	6 (43%)	1 (7%)
Interstitial inflam, >0	27 (44%)	24 (39%)	8 (36%)	6 (27%)	10 (40%)	15 (60%)	9 (64%)	3 (21%)
Chronicity index								
Glomerular sclerosis, >0	25 (41%)	48 (79%)	7 (32%)	17 (77%)	8 (32%)	20 (80%)	10 (71%)	11 (78%)
Fibrous crescents, >0	27 (44%)°	31 (51%)	10 (45.5%)	13 (59%)	12 (48%)	14 (56%)	5 (36%)	(36%)
Tubular atrophy, >0	10 (16%)	38 (63%)°	4 (18%)	11 (50%)	2 (8%)	16 (67%)°	4 (28.5%)	11 (78%)
Interstitial fibrosis, >0	21 (34%)	48 (79%)	8 (36%)	14 (64%)	5 (20%)	22 (88%)	8 (57%)	12 (86%)

° 1 data missing

Legend: Endocap. Hypercell, Endocapillary hypercellularity; Neutr infiltr/karyor, Neutrophils infiltration/karyorrhexis; Cell/fibrocell cresc, Cellular/fibrocellular crescents; Fibr necr, Fibrinoid necrosis; Interstitial inflam, Interstitial inflammation

Supplementary table 2: Histological transformation of lupus nephritis classes between the first and second kidney biopsy

Histological classes at 1st kidney biopsy	Histological classes at 2nd kidney biopsy					
	I (1 pts)	II (6 pts)	III (12 pts)	IV (36 pts)	V (6 pts)	Transformation
III = 7 pts		1 (14%)	3 (43%)	3 (43%)		**57 %**
IV = 47 pts	1 (2%)	5 (10%)	6 (13%)	31 (66%)	4 (9%)	**34%**
V = 7 pts			3 (43%)	2 (28.5%)	2 (28.5%)	**71.5%**
Tot 61 pts						**47%**

Supplementary table 3: Clinical and histological data at first and second kidney biopsy of patients who developed and of those who did not develop kidney function impairment (KFI).

	KFI (n=25)	**NO KFI (n=33)**	**P**
Clinical data at first kidney biopsy			
Serum Creatinine (mg/dl)	1.1 [0.7-1.6]	1.2 [0.9-1.6]	0.718
eGFR (ml/min/1.73m^2)	67 [43-120]	58 [45-86]	0.144
Proteinuria > 3.5 g/die, n° of pts (%)	13 (52%)	14 (42%)	0.469
Arterial hypertension, n° of pts (%)	10 (40%)	22 (67%)	0.043
Histological data at first kidney biopsy			
Activity index	7 [4.5-9]	7 [5.5-10]	0.402
Endocapillary hypercellularity** >1, pts (%)	15 (60%)	18 (54.5)	0.677
Neutrophils infiltration/karyorrhexis** >1, pts (%)	12 (48%)	17 (51.5%)	0.790
Cellular/fibrocellular crescents** >1, pts (%)	6 (24%)	3 (9%)	0.120
Hyaline deposits/wire loops **>1, pts (%)	14 (56%)	21 (63.6%)	0.556
Fibrinoid necrosis** >1, pts (%)	5 (20%)	11 (33%)	0.260
Interstitial inflammation** >1, pts(%)	3 (12%)	6 (18%)	0.519
Chronicity index	1 [1-3]	2 [0-3]	0.646
Glomerular sclerosis** >1, pts (%)	3 (12%)	3 (9%)	0.718
Fibrous crescents** >1, pts (%)	2 (8%)	1 (3%)	0.397
Tubular atrophy** >1, pts (%)	1 (4%)	1 (3)%	0.841
Interstitial fibrosis** >1, pts (%)	3 (12%)	1 (3%)	0.181
Clinical data at second kidney biopsy			
Serum Creatinine (mg/dl)	1.4 [1-2.2]	1 [0.9-1.2]	**0.007**
eGFR (ml/min/1.73m^2)	49 [32-67]	75 [56-97]	**0.023**
Proteinuria > 3.5 g/die	14 (56%)	7 (21%)	**0.006**
Arterial hypertension, n° of pts (%)	17 (68%)	14 (42%)	**0.053**
Nephritic syndrome	16 (64%)	7 (21%)	**0.001**
Histological data at second kidney biopsy			
Activity index	4 [2.5 – 6.5]	1 [1-5]	**0.032**
Endocapillary hypercellularity** >1, pts (%)	15 (60%)	18 (54.5)	0.678
Neutrophils infiltration/karyorrhexis** >1, pts (%)	12 (48%)	17 (51.5%)	0.791
Cellular/fibrocellular crescents** >1, pts (%)	6 (24%)	3 (9%)	0.120
Hyaline deposits/wire loops** >1, pts (%)	14 (56%)	21 (63.6%)	0.556
Fibrinoid necrosis** >1, pts (%)	5 (20%)	11 (33%)	0.260
Interstitial inflammation** >1, pts(%)	3 (12%)	6 (18%)	0.519
Chronicity index	5 [2-7]	4 [2-5]	**0.027**
Glomerular sclerosis** >1, pts (%)	9 (36%)	5 (15%)	0.066
Fibrous crescents** >1, pts (%)	6 (24%)	4 (12%)	0.235
Tubular atrophy** >1, pts (%)	8 (32%)	5 (15%)	0.127
Interstitial fibrosis** >1, pts (%)	10 (40%)	6 (18%)	0.065

P values are evaluated with t-test for independent samples and with Chi-square test between qualitative or dichotomized variables.
(Data of three patients are missing)
** These variables were categorized as: 0+1 vs 2+3, being: 0 if absent; 1+ if mild (in less than 25% of glomeruli and/or in tubulointerstitial cortex); 2+ if moderate (in between 25% and less than 50% of glomeruli and/or in tubulointerstitial cortex), and , 3+ if severe (in more than 50% of glomeruli and/or in tubulointerstitial cortex).

Supplementary Table 4: Clinical and histological predictors of kidney function impairment (KFI) within five years after the second kidney biopsy. Univariate and multivariate analysis.

	Univariate analysis			Multivariate analysis		
	OR	CI	P	OR	CI	P
Clinical features at first kidney biopsy						
Proteinuria >3.5 g/die	3.677	0.995-13.588	0.051			
Histological features at first kidney biopsy						
Cellular/fibrocellular crescents >1**	8.212	2.707-24.909	0.000			
Clinical features at second kidney biopsy						
Serum creatinine	2.387	1.719-3.316	0.000			
Proteinuria >3.5 g/die	3.070	1.004-9.390	0.049			
Histological features at second kidney biopsy						
Cell/fibrocell crescents>1**	10.577	2.836-39.444	0.000	31.955	5.160-197.910	0.000
Interstitial inflammation>1**	3.695	1.128-12.108	0.031			
Chronicity Index >4	23.698	3.075-182.613	0.001	39.078	4.375-349.071	0.001
Fibrous crescents>1**	5.602	1.873-16.754	0.002			
Interstitial fibrosis>1**	6.545	2.129-20.118	0.026			
Tubular atrophy>1**	6.626	2.214-19.832	0.001			

**These variables were categorized as: 0+1 vs 2+3, being: 0 if absent; 1+ if mild (in less than 25% of glomeruli and/or in tubulointerstitial cortex); 2+ if moderate (in between 25% and less than 50% of glomeruli and/or in tubulointerstitial cortex), and , 3+ if severe (in more than 50% of glomeruli and/or in tubulointerstitial cortex).

Supplementary Table 5: Combination of the different risk factors that contributed to the study end-points.

Chronicity indices increase from first to second biopsy. **Clinical /therapeutical predictors**	**Long-term kidney function impairment.** **Clinical and histological predictors**
At first kidney biopsy Serum creatinine ≥ 1.6 mg/dl Presentation with nephritic syndrome Cyclophosphamide tends to protect from chronicity index increase	**At first kidney biopsy** Moderate/severe cellular/fibrocellular crescents
Time dependent factors Renal flares and in particular nephritic flares	**At second kidney biopsy** Serum creatinine Nephrotic proteinuria Arterial hypertension Activity index ≥3 - Moderate/severe cellular/fibrocellular crescents - Moderate/severe hyaline deposits Chronicity index >4 - Moderate/severe fibrous crescents - Moderate/severe interstitial fibrosis