

1 **Table 1. Different groups' demographic and clinical characteristics at biopsy**

Characteristic	All patients (n=40)	MIg (n=6)	HBV/HCV (n=8)	MIg+ HBV/HCV (n=8)	MIg/HBV/HCV negative(n=18)	Pvalue
Sex (M/F)	24/16	5 / 1	5 / 3	4 / 4	10/ 8	0.922
Age(years)*	47.8±14.9	65.8±6.6 ^{bc}	46.5±9.2	45.4±12.4	43.5±16.2	0.008
Course of renal Disease(months) [#]	12.0 (3.0-45.0)	9 (1.6-12)	12 (12-78.0)	18 (6.0-63.0)	3.5 (1.0-72.0)	0.208
Hypertension	28 (70)	6 (100)	6 (75)	6 (75)	10 (55.6)	0.105
Anemia	30 (75)	6 (100)	7 (87.5)	6 (75)	11 (61.1)	0.116
HBV infection	12 (30)	0	6 (75)	6 (75)	0	1.000
Hematological malignancy §	6 (14.3)	2 (25)	1 (12.5)	0	3 (16.7)	0.361
Purpura	9 (22.5)	1 (16.7)	3 (37.5)	4 (50) ^f	1 (5.62)	0.049
Arthralgia	5 (12.5)	1 (16.7)	0	2 (25)	2 (11.11)	0.365
Renal insufficiency	23 (57.5)	6 (100) ^a	3 (37.5)	5 (62.5)	9 (50)	0.038
Nephrotic proteinuria	23 (57.5)	4 (66.7)	3 (37.5)	5 (62.5)	11 (61.1)	0.641
Microscopic hematuria	38 (95)	6 (100)	7 (87.5)	8 (100)	17 (94.4)	0.546
Serum creatinine (mg/dL) [#]	1.41 (0.99-2.48)	2.51 (2.18-3.34) ^{ac}	1.06 (0.89-2.66)	1.38 (1.10-3.62)	1.24 (0.93-1.98)	0.071
eGFR(ml/min per 1.73m ²) [#]	50.0 (26.4-75.7)	25.6 (20.8-29.0) ^{ac}	74.6 (25.3-99.0)	48.8 (18.2-74.0)	61.3 (36.5-77.3)	0.054
Urine protein (g/24 h) [#]	3.9 (1.8-6.6)	4.9 (1.4-5.8)	2.2 (1.5-4.0)	5.1 (1.3-6.7)	4.1 (2.8-7.6)	0.340
Cryoglobulins concentration(mg/L) [#]	1175 (810-2303)	2440 (816-2858)	1459 (884-2303)	954 (679-2425)	1140 (822-1783)	0.509
Abnormal serum FLC ratio	16(43)	2(33.3)	3(37.5)	6(75)	5(27.8)	0.148
Decrease of C3 level	25 (62.5)	4 (66.7)	7 (87.5)	5 (62.5)	9 (50)	0.293
Decrease of C4 level	14 (35)	3 (50)	4 (50)	4 (50)	3 (16.7)	0.166
Combined decreased of C3 and C4 levels	12 (30)	3 (50)	4 (50)	3 (37.5)	2 (11.1)	0.097
Increase of RF titers	26 (65)	1 (16.7) ^a	8 (100)	7 (87.5) ^b	10 (55.6) ^d	0.001
Follow-up (months) [#]	24.9 (2.6-40.4)	13.6 (1.2-45.7)	24.1 (5.2-48.4)	2.1 (1.0-89.4)	30.3 (16.8-38.2)	0.616
Renal survivals (months) [#]	22.1 (2.3-34.5)	12.5 (0.3-40.8)	24.1 (5.2-48.4)	7.0 (1.0-42.1)	26.3 (14.2-32.3)	0.463
Progressed to ESRD	11 (28.9%)	4 (66.7) ^a	0 (0)	3 (37.5)	4 (22.2)	0.021

2 *: Data are shown as mean ± SD. #: Data are given as median (interquartile range). The remaining data
3 are given as number (percentage). §: Bone biopsy shows hematologic malignancy in 6 cases, including
4 B-cell lymphoma (n=3), lymphoplasmacytic lymphoma (n=1) and 2 cases not being excluded from small
5 B lymphoproliferative disorders. a:MIg vs HBV/HCV, $P<0.05$; b: MIg vs MIg+ HBV/HCV, $P<0.05$;
6 c: MIg vs MIg/HBV/HCV negative, $P<0.05$; d: HBV/HCV vs MIg/HBV/HCV negative, $P<0.05$;

8 **Table 2. Histopathologic characteristics of different groups**

	All patients (n=40)	MIg (n=6)	HBV/HCV (n=8)	MIg+HBV/HCV (n=8)	MIg/HBV/HCVnegative (n=18)	Pvalue
<i>Histologic pattern</i>						
MPGN	38 (92.5)	6 (100)	8 (100)	6 (67.5)	18 (100)	0.949
EPGN	2 (7.5)	0	0	2 (25)	0	
<i>Light microscopy</i>						
globally sclerotic glomeruli	24 (60)	3 (50)	4 (50)	3 (37.5)	14 (77.8)	0.189
Percentage of globally sclerotic glomeruli	14 (5.5-23)	(3,10,18) &	5 (3-8.5) ^d	(5,10,24) &	16 (13.5-27)	0.070
PAS positive cryo-Plugs	10 (25)	4 (66.7)	1 (12.5)	2 (25)	3 (16.7)	0.107
Score of acute tubular lesion	1.0 (1.0-2.0)	2.0 (0.75-2.25)	1.0 (0.25-1.0)	1.0 (1.0-1.25)	1.0 (1.0-2.0)	0.447
Score of TA/IF	1.0 (1.0-1.0)	1.5 (1.0-2.0) ^{abc}	1.0 (0.25-1.0)	1.0 (0.75-1.0)	1.0 (0.75-1.0)	0.075
<i>Immunofluorescence</i>						
Deposition of IgG IgA IgM	19 (47.5)	2 (33.3)	4 (50)	4 (50)	9 (50)	0.901
Deposition of IgG IgA	2 (5)	0	0	0	2 (11.1)	—
Deposition of IgG IgM	11 (27.5)	2 (33.3)	2 (25)	3 (37.5)	4 (22.2)	0.858
Deposition of IgM	5 (13.9)	1 (16.7)	2 (25)	1 (12.5)	1 (7.1)	0.712
Deposition of IgG	3 (7.5)	1 (16.7)	0	0	2 (11.1)	0.341
Organized deposits on EM	11 (32.4)	4 (66.7)	2 (33.3)	1 (14.3)	4 (26.7)	0.222

9 &: data is not enough to calculate median and is listed here. TA/IF: tubular atrophy and interstitial fibrosis.
10 a:MIg vs HBV/HCV, $P < 0.05$; b: MIg vs MIg+ HBV/HCV, $P < 0.05$; c: MIg vs MIg/HBV/HCV negative,
11 $P < 0.05$; d: HBV/HCV vs MIg/HBV/HCV negative, $P < 0.05$.

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Table 3. Immunofluorescence of patients with MIg in serum and/or single Ig deposits, or sole IgG subtype deposits

Groups(n)	No.	SIFE results	Glomerular Ig deposits	IgG subtype	Light-chain deposits	Organized deposits on EM	Results of bone biopsy
MIg (n=6)	1	IgGκ	IgG IgM C3	IgG1, IgG3	κ λ	No	N
	2	IgMκ	IgM C3	—	κ	Curved microtubules	Small B cell lymphoproliferative disorder
	3	IgGκ	IgG C3	IgG3	κ	Special structure*	Plasmacyte infiltration 2%
	4	IgGλ	IgG IgA IgM C3	IgG1	κ λ	Packed fibrils	N
	5	IgMκ	IgM IgG C3 C1q	IgG1, IgG2	κ λ	Curved microtubules	N
	6	IgMκ	IgG IgA IgM C3	ND	κ λ	No	Small B-cell lymphoma
MIg+HBV/HCV (n=8)	7(HCV)	IgMκ	IgM C3	—	κ	No	ND
	8(HCV)	IgMκ	IgG IgA IgM C3	ND	ND	No	ND
	9	κ	IgG IgM C3	IgG1-4	κ λ	No	N
	10	IgGκ	IgG IgA IgM C3	ND	ND	ND	N
	11	IgMκ	IgG IgM C3	ND	κ λ	No	N
	12	IgMκ	IgG IgM C3	IgG1-4	κ λ	No	Plasmacyte infiltration 5%
	13	λ	IgG IgA IgM C3	IgG1-4	κ λ	No	ND
	14	IgGκ	IgG IgA IgM C3	IgG1-4	κ λ	fingerprint structure	ND
HBV/HCV (n=2)	15(HCV)	—	IgM C3 C1q	—	κ λ	ND	ND
	16(HCV)	—	IgM C3 C1q	—	κ λ	No	Small B cell lymphoproliferative disorder
MIg/HBV/HCV negative (n=5)	17	—	IgG C3 C1q	IgG3	κ λ	No	N
	18	—	IgG IgM C3 C1q	IgG3	κ λ	No	Plasmacyte infiltration 2.4%
	19	—	IgG IgM C3	IgG3	κ	No	N
	20	—	IgM C3	—	κ λ	ND	B-cell lymphoma

SIFE: serum immunofixation electrophoresis. Ig: immunoglobulin. EM: electron microscope. ND: IgG subtype was not performed or no data. *: deposits were identified as hollow lattice structure curved at both ends, some cross sections were concentric circle like. N: no abnormalities.

31 **Table 4. Cox analysis of variables predicting renal survival**

Parameters	Univariate analysis		Multivariate analysis	
	<i>P</i> value	HR (95%CI)	<i>P</i> value	HR (95%CI)
Age	0.039	1.052(1.003-1.104)		
Renal insufficiency	0.096	3.684(0.794-17.098)		
Positive serum MIg	0.010	5.090(1.481-17.50)	0.034	47.881(1.33-1723.681)
Decrease of C3 level	0.073	0.296(0.078-1.119)		
eGFR	0.083	0.083(0.961-1.002)		
Increase of RF titers	0.018	0.222(0.064-0.772)		
Nephrotic proteinuria	0.074	4.092(0.872-19.196)		
Urine NAG	0.071	1.029(0.998-1.062)		
globally sclerotic glomeruli	0.087	3.870(0.822-18.220)	0.064	10.957(0.872-137.679)
globally sclerotic glomeruli (%)	0.020	32.069 (1.732-593.813)		
Score of TA/IF	0.002	7.558 (2.037-28.035)		

32 TA/IF: tubular atrophy and interstitial fibrosis

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Patient No.	Therapy	Follow-up(month)	Renal response (CR/PR/NR)
Mlg group			
1	CS+CTX	41.8	NR(ESRD)
2*	TD	1	Died of unknown complication
3	TD	2.6	NR(ESRD)
4	BD	24.6	NR(ESRD)
5	CS+CTX	57.5	NR
6#	CS+CTX	1.3	NR(ESRD)
HBV/HCV group			
7	IFN	19.1	PR (positive cryoglobulin)
8*	IFN+RBV+TW	71.7	PR
9	CS+TW	38.2	NR
10	CS+RTX	2.6	NR
11	CS+ETV	29.1	PR
12	TW	12.9	CR
13	CS+ETV	1.1	NR
14	LAM	51.8	PR
Mlg+HBV/HCV group			
15	CS	ND	ND
16	IFN+RBV+RTX	1.3	PR
17	None\$	1.0	NR
18	CS+CTX	2.1	Dialysis at renal biopsy
19	ETV+IFN	0.8	NR(ESRD)
20	ETV+MMF+TW	101.5	NR(ESRD)
21	ETV	12.6	NR(ESRD)
22	ETV	89.4	PR
Mlg/HBV/HCV negative			
23	CS	55.0	CR (positive cryoglobulin)
24	CS	29.4	NR
25	CS+LFM	34.2	NR
26	None\$	45.3	NR(ESRD)
27	CS	40.4	PR
28	CS+TW	31.2	NR(ESRD)
29	CS	14.4	NR
30	CS+TW	1.1	NR
31	CS	27.8	PR
32	CS+TW	18.7	NR(ESRD)
33	CS+FK506	37.4	NR(ESRD)
34	CS	1	NR
35	CS+TW	5.3	NR
36&	CS	24.9	NR
37	CS+CTX	31.6	NR

Patient No.	Therapy	Follow-up(month)	Renal response (CR/PR/NR)
38	CS+FK506	31.4	NR
39#	CS	17.6	PR
40#	CS+TW	142.4	NR

*: small B lymphoproliferative disorders cannot be ruled out. #: B-cell lymphoma. &: lymphoplasmacytoid cell lymphoma. \$: patient received symptomatic treatment. CS:corticosteroids, CTX: cyclophosphamide, TD: thalidomide and dexamethasone, BD: bortezomib and dexamethasone, LAM: lamivudine, IFN: interferon, RBV: ribavirin, ETV: entecavir, TW: Tripterygium Wilfordii, RTX: rituximab, MMF: mycophenolate mofetil, LFM: leflunomide. PR: partial remission, CR: complete remission, NR: non-responder. ESRD: end-stage renal disease. ND: Loss of follow-up.

43 **Table6. Clinicopathologic features and outcome in this study and previous reports**

	Tarantino [1] (n=105)	Roccatello [2] (n=146)	Matignon[3] (n = 20)	Zaidan [4] (n = 80)	This study (n = 40)
HCV infection n(%)	29 (85)	129 (88)	0	0	4 (10)
Hematological malignancy n(%)	0	ND	1 (5)	23 (28.7)	6 (15)
Autoimmune disease n(%)	0	ND	9 (45)	18 (22.5)	0
Age at diagnose(years)	52.7±10.65	52.2 ±13	60±12	62.6±14.1	47.8±14.9
Woman (%)	59	56.8	60	62.5	40
Hypertension (%)	82%	55	80	85.3	70
Decrease of C4 level (%)	ND	>76	95	75.4	35
Decrease of C3 level (%)	ND	>41	10	ND	62.5
Renal insufficiency (%)	47%#	58	85	82.3	57.5
Microscopic hematuria (%)	55%	88	100	97.4	95
Nephrotic proteinuria (%)	20%	21	75	49.4	57.5
eGFR<60(%)	ND	56	85	82.3	42.5
MPGN (%)	80%	80	100	92.5	92.5
Time of follow up(months)	72(1-283)	97.2(average)	48 (3-264)	49.9±45.5	24.9 (2.6-40.4)
independent risk factors of ESRD	Age, purpura , splenomegaly, serum levels of C3,Scr, cryocrit.	Age, serum levels of Scr and proteinuria	ND	Dialysis at diagnosis, extracapillary proliferation	Positive serum MIg
Possessing to ESRD (%)	14.3*	11.1 [¥]	10	9	28.9

44 #: increase of serum creatinine levels. *: chronic renal functional failure: serum creatinine levels >
45 4mg/dL, for at least six consecutive months. ¥: including 5 patients on dialysis therapy. ND: no data.

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47 **Reference**

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