Appendix

	Table of Contents for Supplemental Information
1	List of Investigators
2	Assessments of Clinical Parameters
3	Supplemental Figures
4	Supplemental Tables

1. List of investigators

Haitao Zhang, Zhengzhao Liu, Minlin Zhou, Caihong Zeng and Zhihong Liu, National Clinical Research Center of Kidney Diseases, Jinling Hospital, Nanjing University School of Medicine, Nanjing, China;

Zhangsuo Liu and Zhaohui Zheng, The First Affiliated Hospital, Zhengzhou University, Zhengzhou, China;

Jianghua Chen and Heng Li, The First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China;

Changying Xing, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China;

Hongli Lin and Longkai Li, The First Affiliated Hospital of Dalian Medical University, Dalian, China;

Zhaohui Ni and Shan Mou, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;

Ping Fu and Zhangxue Hu, West China Hospital, Chengdu, China;

Fuyou Liu and Yinghong Liu, The Second Xiangya Hospital of Central South University, Changsha, China;

Nan Chen and Hong Ren, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China;

Yongcheng He and Yi Xu, Shenzhen Second People's Hospital, Shenzhen, China;

Jianshe Liu and, Hongyan Zhu, Wuhan Union Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China;

Yani He and Bengang Huo, Daping Hospital, Third Military Medical University, Chongqing, China;

Wei Shi and Zhiming Ye, Guangdong General Hospital, Guangzhou, China;

Weijie Yuan and Minghua Shang, Shanghai First People's Hospital, Shanghai, China;

Guohua Ding and Hongyan Liu, Renmin Hospital of Wuhan University, Wuhan, China;

Ying Li and Qiongzhen Lin, The Third Hospital of Hebei Medical University, Shijiazhuang, China;

Junzhou Fu and Xiaojun Lin, Guangzhou First People's Hospital, Guangzhou, China;

Yong Gu and Jun Xue, Huashan Hospital, Shanghai, China;

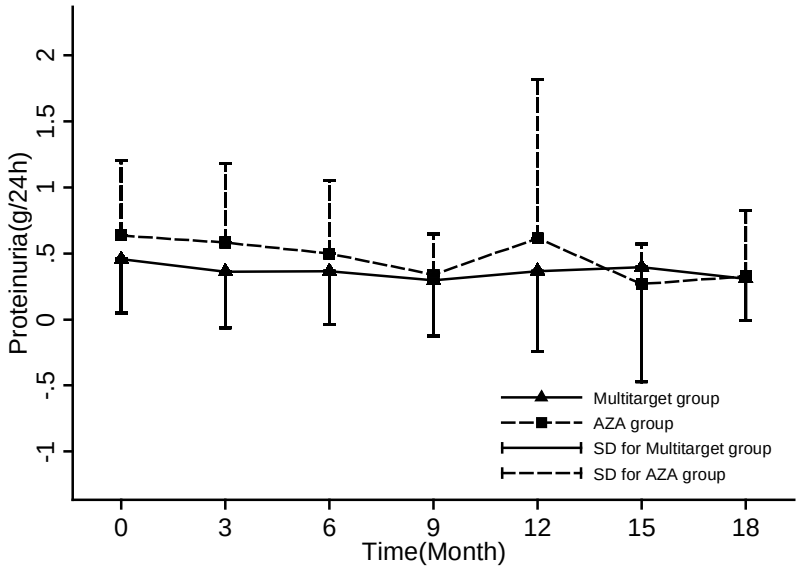
Wenhu Liu and Wang Guo, Beijing Friendship Hospital, Beijing, China.

2. Assessments of Clinical Parameters

The 24-h urinary protein concentration was measured using the biuret colorimetric method after patients had partaken of a normal diet for three days before testing and avoided using diuretics and albumin. Serum albumin levels were measured using the bromocresol green method. SCr levels were measured using an enzymatic method. N-acetyl-beta-D- glucosaminidase (NAG) concentrations were determined using an enzyme-substrate colorimetric method, and retinol binding protein (RBP) levels were measured using an ELISA. The estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.

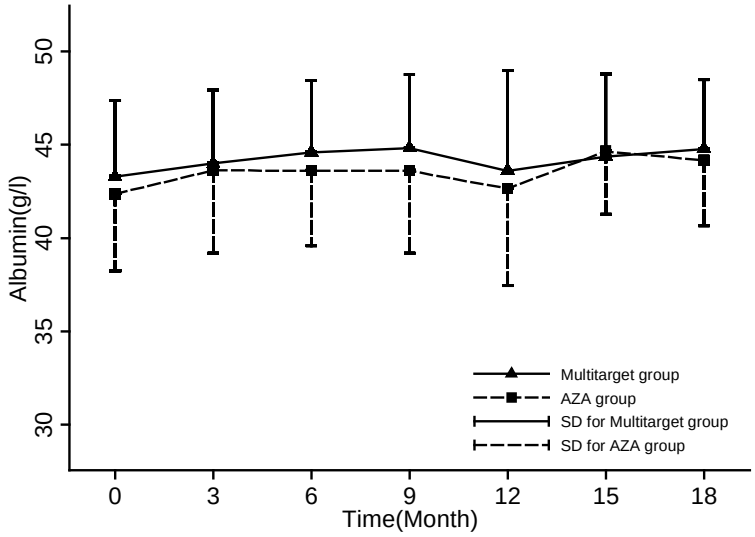
3. Supplemental Figures

Supplemental Figure 1A. Changes in proteinuria during the maintenance treatment.



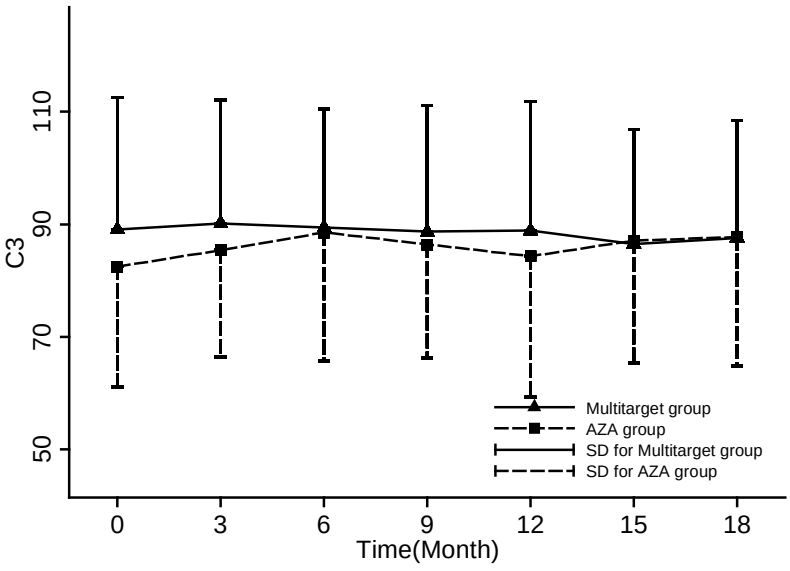
Multitarget group vs. AZA group, P=0.072

Supplemental Figure 1B. Changes in serum albumin levels during the maintenance treatment.



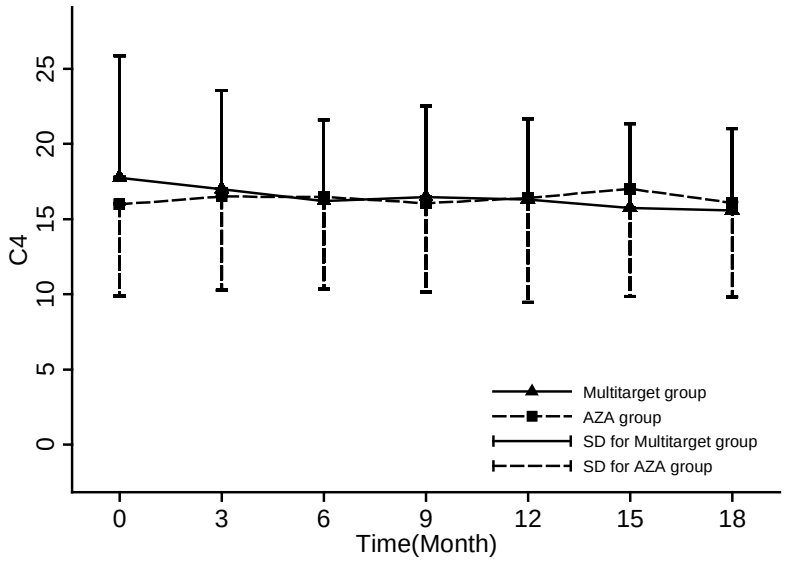
Multitarget group vs. AZA group, P=0.271

Supplemental Figure 1C. Changes in serum C3 levels during the maintenance treatment.



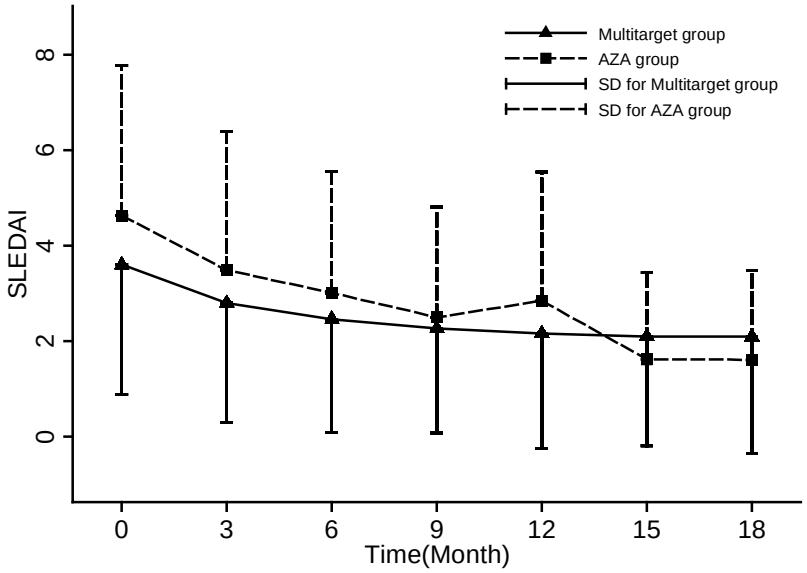
Multitarget group vs. AZA group, P=0.359

Supplemental Figure 1D. Changes in serum C4 levels during the maintenance treatment.



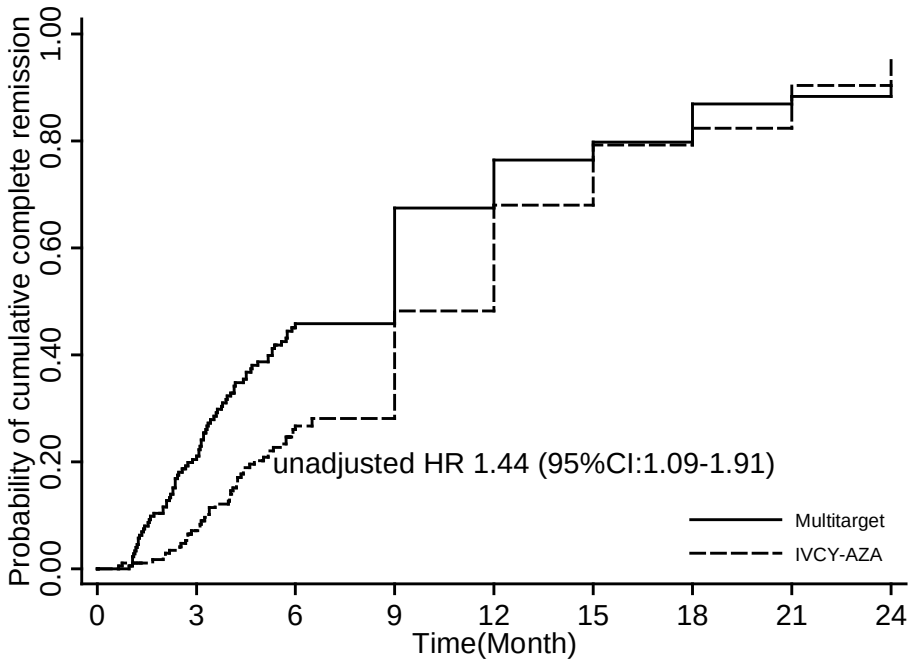
Multitarget group vs. AZA group, P=0.477

Supplemental Figure 1E. Changes in SLEDAI during the maintenance treatment.



Multitarget group vs. AZA group, P=0.023

Supplemental Figure 2. The cumulative probability of achieving CR during multitarget therapy and IVCY-AZA treatments. Cumulative CR data were analyzed using Kaplan-Meier curves and between-group differences were compared using the log-rank test. The frailty model was used to estimate the HRs.

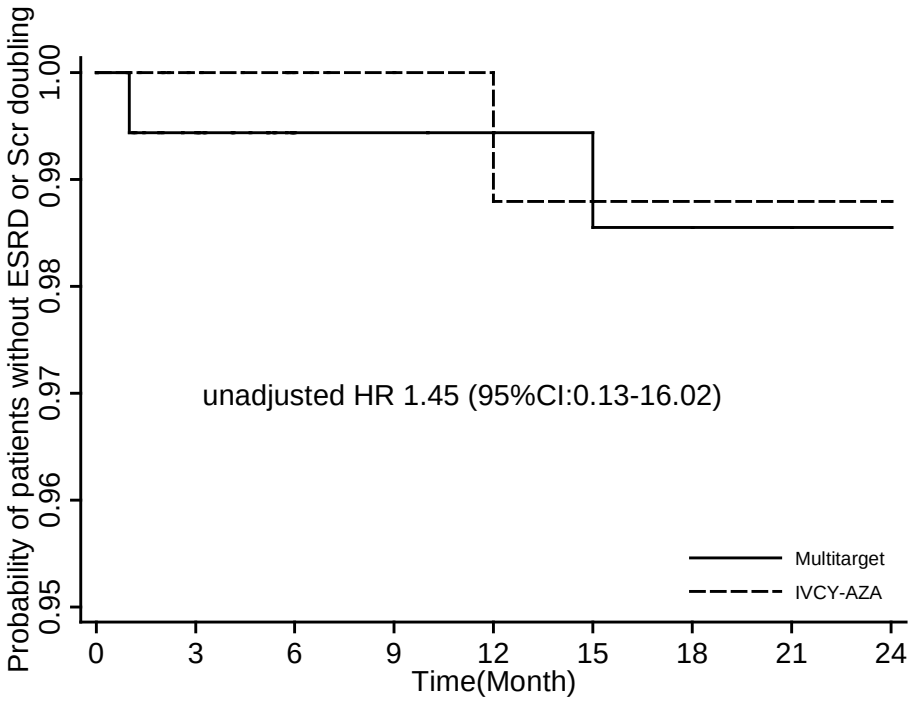


No. at risk									
Multitarget	181	132	80	50	29	21	17	9	7
IVCY-AZA	181	152	108	50	34	20	13	11	5
No. with complete remission									
Multitarget	0	36	39	20	8	3	6	1	1
IVCY-AZA	0	12	31	15	13	7	2	5	3

Log-rank test statistic 7.69, *P*=0.006

IVCY = intravenous cyclophosphamide therapy; AZA = azathioprine

Supplemental Figure 3. The probability of patients without ESRD or SCr doubling during multitarget therapy and IVCY-AZA treatments. ESRD or SCr doubling data were analyzed using Kaplan-Meier curves and between-group differences were compared using the log-rank test. The frailty model was used to estimate the HRs.



No. at risk									
Multitarget	181	166	148	148	113	112	108	103	101
IVCY-AZA	181	164	147	87	83	75	71	66	64
No. of ESRD or SCr doubling									
Multitarget	0	1	0	0	0	1	0	0	0
IVCY-AZA	0	0	0	0	1	0	0	0	0

Log-rank test statistic 0.142, *P*=0.706

IVCY = intravenous cyclophosphamide therapy; AZA = azathioprine

4. Supplemental Tables

Supplemental Table 1. Reasons for premature withdrawal from the maintenance treatment

	Multitarget (n=116)			AZA (n=90)		
	Event no.	Crude rate, %	Rate (per 100 patients-year)	Event no.	Crude rate, %	Rate (per 100 patients-year)
Patient didn't complete 18 month follow-up **	15	12.9	9.15	26	28.9	23.12
Follow-up time (months), median (IQR)	12 (6, 12)			6.5 (3, 12)		
Relapse	6	5.2	3.66	7	7.8	6.22
Renal relapse†	6	5.2	3.66	6	6.7	5.34
Extra-renal relapse	0	0	0	1	1.1	0.89
Reaching renal endpoint events ‡	3	2.6	1.83	3	3.3	2.67
ESRD	1	0.9	0.61	0	0	0
Sustained doubling of SCr	2	1.7	1.22	1	1.1	0.89
eGFR decreased ≥30%	1	0.9	0.61	2	2.2	1.78
Death	0	0	0	0	0	0
Reasons for dropout**	9	7.8	5.49	20	22.2	17.78
Lost to follow-up	7	6.0	4.27	10	11.1	8.89
Withdrawal due to adverse events*	2	1.7	1.22	8	8.9	7.11
Protocol violation	0	0	0	2	2.2	1.78

The crude rates were compared using Fisher's exact method, * P<0.05; ** P<0.01.

ESRD = end stage renal disease

† One patient in the AZA group experienced renal relapse at the 18th month.

‡ One patient in the multitarget group experienced simultaneous doubling of SCr level and ESRD.

Supplemental Table 2. Subgroup analysis of renal relapse according to the baseline renal response

Remission status	Group	Event no.	Cumulative relapse rate and 95%CI	*P* value	Unadjusted HR and 95%CI	adjusted HR and 95%CI
CR	**Multitarget** (n=69)	3	4.55 (1.49, 13.43)	0.721	0.727 (0.122, 4.352)	0.601 (0.100, 3.605)
	AZA (n=40)	2	6.25 (1.60, 22.75)			
PR	**Multitarget** (n=47)	3	6.93 (2.29, 19.96)	0.657	0.711 (0.156, 3.239)	0.811 (0.170, 3.876)
	AZA (n=50)	4	8.85 (3.39, 22.04)			

CR = complete remission; PR= partial remission

Supplemental Table 3. Dose and blood trough concentration of tacrolimus during the maintenance treatment

Variable, mean (SD)	Visit Time						
	Month 0	Month 3	Month 6	Month 9	Month 12	Month 15	Month 18
Dose of tacrolimus (mg/d)	3 .0	3.0	3 .0	2 .0	2 .0	2 .0	2.0
Blood trough concentration of tacrolimus (ng/mL)	5.71±2.93 (n=56)	4.94±2.24 (n=36)	4.46±2.15 (n=21)	4.24±1.29 (n=12)	3.37±1.08 (n=9)	3.23±1.37 (n=7)	3.55±1.20 (n=8)

Supplemental Table 4. Changes in urinary NAG and RBP levels

	Multitarget			AZA		
	Before Treatment	**After Treatment**	***P* value**	**Before Treatment**	**After Treatment**	***P* value**
NAG (U/gCr)	6.97±4.76 (37)	5.91±6.62 (38)	0.739	5.30±2.58 (13)	5.42±4.60 (20)	0.174
RBP (mg/L)	0.43±0.34 (37)	0.30±0.32 (39)	0.899	0.55±0.31 (13)	0.72±0.36 (20)	0.212

NAG = N-acetyl-beta-D-glucosaminidase; RBP = retinol binding protein

Supplemental Table 5. Aggregated data on adverse events observed in both the induction and maintenance phases of the study

Type of Adverse Event	Multitarget (n =181)		IVCY-AZA (n =181)		*P* value
	Event no.	Crude rate,%	Event no.	Crude rate,%	
All	101	55.8	113	62.4	0.240
Infection	60	33.2	51	28.2	0.362
Varicella zoster virus	14	7.7	7	3.9	0.176
Herpes simplex	4	2.2	4	2.2	1.000
Pneumonia	13	7.2	5	2.8	0.088
Urinary tract infection	3	1.7	6	3.3	0.502
Skin and soft tissue infection	1	0.6	4	2.2	0.372
Upper respiratory tract infection	29	16.0	25	13.8	0.658
Other infections	6	3.3	3	1.7	0.502
Upper gastrointestinal symptoms**	8	4.4	41	22.7	<0.0001
Diarrhea	14	7.7	6	3.3	0.105
Liver dysfunction*	2	1.1	12	6.6	0.011
Hyperglycemia	5	2.8	4	2.2	1.000
New-onset hypertension	10	5.5	4	2.2	0.171
Myalgia	2	1.1	0	0	0.499
Headache	3	1.7	0	0	0.248
Alopecia	6	3.3	9	5.0	0.599
Leukopenia**	9	5.0	33	18.2	0.0001
Tremor*	8	4.4	1	0.6	0.037
Menstrual disorder	2	1.1	9	5.0	0.061
Gingival hyperplasia	2	1.1	0	0	0.499
Osteonecrosis	2	1.1	1	0.6	1.000
Arthralgia	3	1.7	1	0.6	0.623
Doubling of SCr level	2	1.1	0	0	0.499
Thrombocytopenia	1	0.6	0	0	1.000
Others	20	11.0	11	6.1	0.132

The crude rates were compared using Fisher's exact method, *P<0.05; **P<0.01.

IVCY = intravenous cyclophosphamide therapy; AZA = azathioprine