Supplementary Materials

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Jing H, Ruijun Z, Miao S, et al. Efficacy and safety of low-dose Interleukin-2 in the treatment of systemic lupus erythematosus: a randomised, double-blind, placebo-controlled trial.

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Impact of IL-2 therapy on NK cell activity

To verify the phenotypic changes of NK cells and $CD8^+$ T cells after IL-2 therapy, we compared the effects of low-dose IL-2 and conventional therapy on NK cell responses and representative virus-specific responses of CD8 T cells with another prospective, open-labelled study (NCT02932137). Ten patients receiving low-dose IL-2 therapy and ten with standard therapy consented for the evaluation of NK cells and CD8+ T cells. Significant increase of IFN□ (*P*=0.024), NKp46 (*P*=0.025) and NKG2D (*P*=0.003) expression by NK cells were observed after low-dose IL-2 treatment, but not in patients receiving standard therapy (**Table S11**). However, we did not find any significant change in $CD8^+$ T cells after CEF peptide stimulation in IL-2 treated patients and patients under conventional therapy (**Supplementary Table S12**).

To further examine the impact of low-dose IL-2 on infections in SLE patients, 8 patients receiving low-dose IL-2 therapy consented to have their blood screened for infections (30 viruses, **Table S7**)**.** One patient was positive for human papillomavirus and 2 were positive for BK virus at baseline (**Table S6**). The viral titres in patients were measured at week 2 and 10. Despite no anti-viral therapy, the viral loads of these 3 patients decreased to normal at week 10 with low-dose IL-2 treatment (**Table S4**).

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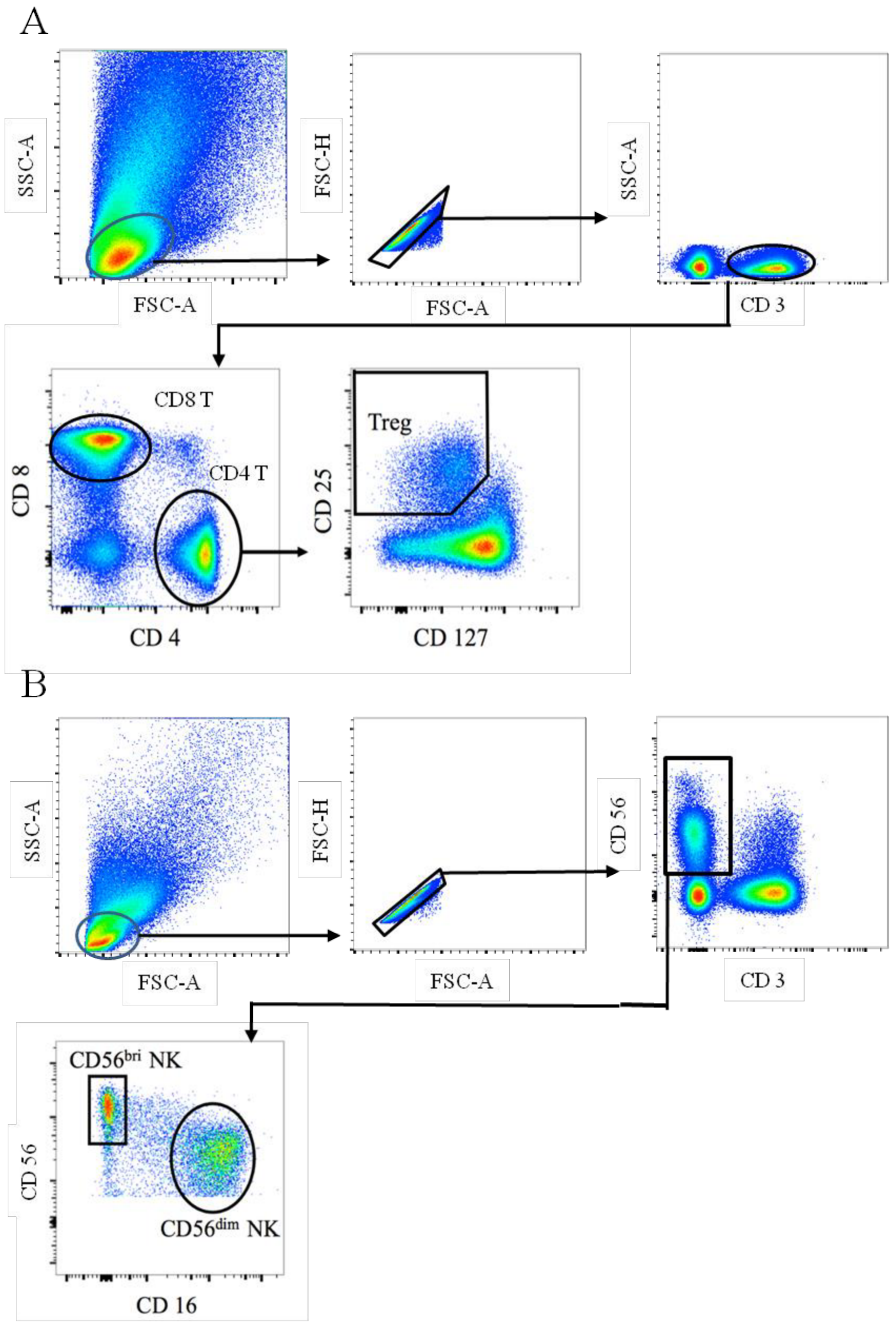
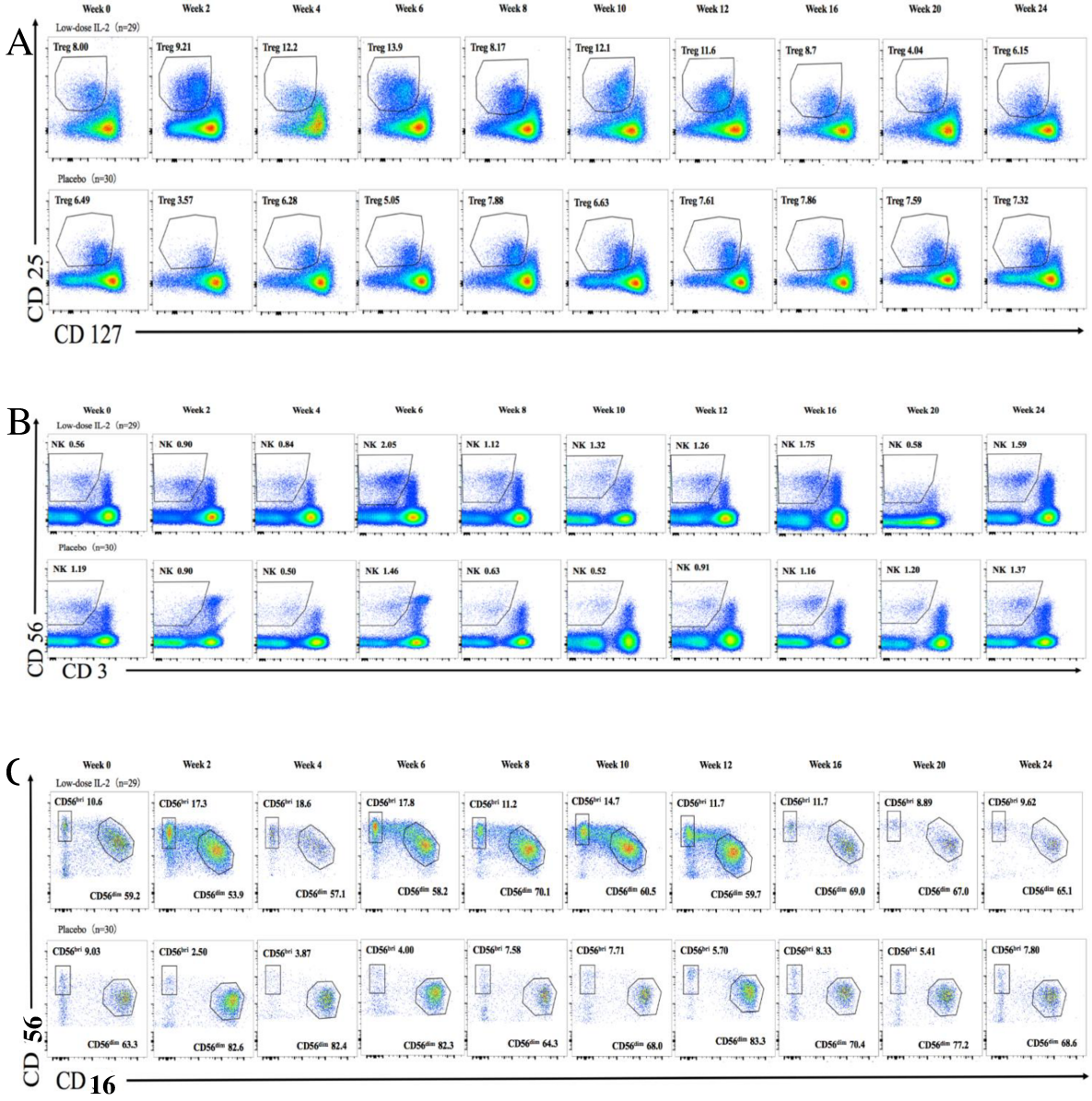
Figure S1. Representative gating of T cell and NK cell subsets



Panel A shows the gating of $CD4^+$, $CD8^+$ and regulatory T cells. Panel B shows the gating of total NK cells ($CD56^+CD3^-$l) and its $CD56^{bri}CD16^-$ and $CD56^{dim}CD16^+$ subsets.

Figure S2. Immune cell subset dynamics during low-dose IL-2 treatment and follow-up



Panel A shows the changes of Treg cell at indicated time during the trial by flow cytometry in low-dose IL-2 group or placebo group. Panel B shows the changes of NK cells. Panel C shows the changes of $CD56^{bri}$ and $CD56^{dim}$ NK cell subsets. The detailed results were show in Table S7.

Table S1. Baseline characteristics of SLE patients in trial NCT02465580 (n=60)

Characteristics	IL-2 (n=30)	Placebo (n=30)	P value
Age, year, mean ±SD	31.58±9.25	29.83±9.72	0.474
Female/Male	27/3	29/1	0.612
Weight, kg, mean ±SD	54.81±8.33	58.69±8.87	0.117
Height, cm, mean ±SD	162.23±6.81	162.67±5.41	0.743
Area, m^2, mean ±SD	1.57±0.140	1.62±0.13	0.708
Duration, year, mean ±SD	66.7±57.4	63.6±59.9	0.652
SLEDAI, median (range)	12 (8, 27)	11 (8, 22)	0.351
Medications			
Prednisone dose, mg/day, median (range)	12.5 (0, 50)	15 (5, 50)	0.331
Hydroxychloroquine	29 (96.67)	28 (93.33)	1.000
Cyclophosphamide	4 (13.33)	0 (0)	0.112
Azathioprine	1 (3.33)	4 (13.33)	0.352
Cyclosporine	0 (0)	5 (16.67)	0.052
Mycophenolate Mofetil	9 (30.00)	8 (26.67)	1.000
Tacrolimus	1 (3.33)	1 (3.33)	1.000
Leflunomide	3 (10.00)	1 (3.33)	0.611
Thalidomide	1 (3.33)	0 (0)	1.000
Methotrexate	1 (3.33)	1 (3.33)	1.000

*For a continuous variable, median (range) and means ±SD, for a categorical variable, count (percentage).

Table S2. Baseline clinical characteristics of the enrolled patients with SLE in the study

ID	Groups	Baseline												
	1= IL-2 2= Placebo	Sex	Age	Duration (m)	Manifestations	SLEDAI	WBC (10^9/L)	PLT (10^9/L)	ANA	Anti-dsDNA (<25.0 IU/ml)	C3 (0.790-1.520g/L)	C4 (0.160-0.380g/L)	Proteinuria (g/day)	Treatment
SLE-1	1	F	26	156	LN, rash	12	7.59	318	0	38.4	0.794	0.205	1.34	Pred 10mg qd HCQ 0.2g bid FK506 1mg tid
SLE-2	2	F	22	1	Arthritis, fever,myalgia	13	3.8	289	640	132.1	0.450	0.050	0.12	Pred 50mg qd HCQ 0.2g bid
SLE-3	1	F	24	2	Arthritis, NPSLE, fever, alopecia	27	3.37	186	320	260.4	0.307	0.048	0.09	Pred 50mg qd HCQ 0.2g bid
SLE-4	2	F	24	9	Arthritis, rash, LN	14	6.7	206	640	321.4	0.326	0.034	1.22	Pred 50mg qd HCQ 0.2g bid
SLE-5	2	M	32	34	LN	10	5.1	142	80	4.3	0.711	0.232	6.54	Pred 7.5mg qd HCQ 0.2g bid AZA 50mg bid
SLE-6	1	F	58	29	Arthritis, rash, alopecia	12	3.5	130	640	35.6	0.672	0.102	0.06	Pred 20mg qd HCQ 0.2g bid

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														Thal 50mg qn
SLE-7	2	F	43	196	Arthritis, LN, rash	22	5.89	185	640	852.97	0.421	0.074	5.75	Pred 50mg qd HCQ 0.2g bid MMF 0.5g bid CsA 50mg tid
SLE-8	1	F	25	108	Thrombocytopenia, arthritis, pericarditis	9	12.18	91	160	14.9	0.712	0.164	0.07	Pred 20mg qd HCQ 0.20g bid MMF 0.75g bid
SLE-9	2	F	21	30	Thrombocytopenia, fever, rash, arthritis	8	7.4	74	80	20.2	0.965	0.184	0.11	Pred 7.5mg qd HCQ 0.2g bid CsA 75mg bid
SLE-10	2	F	24	69	Rash, LN	10	4.89	241	640	223.23	0.356	0.057	0.35	Pred 30mg qd HCQ 0.2g bid AZA 50mg qd
SLE-11	1	M	28	84	LN	16	5.08	215	320	2.6	0.806	0.416	2.14	Pred 10mg qd HCQ 0.2g bid CTX 0.4g q2w
SLE-12	1	F	34	39	Arthritis, myositis, fever, rash	15	5	210	320	60.7	0.513	0.08	0.12	Pred 30mg qd HCQ 0.2g bid MMF 0.5g bid
SLE-13	2	F	38	2	Alopecia, arthritis	8	8.28	239	320	1	0.718	0.169	0.13	Pred 50mg qd CsA 50mg bid HCQ 0.2g bid
SLE-14	2	F	28	32	Arthritis, oral ulcer	8	4.18	324	0	7.7	0.928	0.152	——	Pred 15mg qd HCQ 0.2g bid
SLE-15	1	F	29	14	Vasculitis oral ulcer	16	5.59	323	160	162.8	0.836	0.086	0.04	Pred 25mg qd HCQ 0.2g bid

														MMF 1g bid
SLE-16	1	F	39	36	arthritis, alopecia, rash, oral ulcer	10			160	1.0	0.943	0.176	——	Pred 10mg qd HCQ 0.2g bid
SLE-17	2	F	23	96	LN, rash, NPSLE, thrombocytopenia	15	13.12	93		164	0.514	0.074	2.61	Pred 10mg qd FK506 1g bid AZA 50mg qd
SLE-18	1	F	35	123	Alopecia, rash, arthritis	10	4.85	383		22.6	0.701	0.157	0.12	Pred 5mg qd HCQ 0.2g bid
SLE-19	2	F	47	144	Proteinuria, rash	8	5	170	640	46	1.25	0.208	1.42	Pred 10mg qd HCQ 0.2g bid MMF 1g bid
SLE-20	1	F	22	90	LN	12	3.17	181	320	1783.15	0.735	0.092	1.8	Pred 17.5mg qd CTX 0.4g q2w
SLE-21	2	F	24	123	LN	12	3.47	239	320	129.2	0.431	0.106	1.63	Pred 7.5mg qd HCQ 0.2g bid
SLE-22	1	F	21	60	Rash, fever, thrombocytopeni, leukopenia	9	1.7	58	80	30.9	1.02	0.153	0.13	Pred 50mg qd HCQ 0.2g bid CTX 0.4g q2w
SLE-23	2	F	26	42	Arthritis, rash, leukopenia	11	2.91	144	0	58.5	0.502	0.094	0.12	Pred 5mg qd HCQ 0.2g bid LEF 10mg bid
SLE-24	1	F	41	55	Proteinuria, arthritis, rash	16	5.12	205	320	28.4	1.080	0.163	1.17	Pred 15mg qd HCQ 0.2g bid MMF 0.75g bid
SLE-25	2	F	19	0	Thrombocytopenia, rash, fever	8	9.3	69	640	37.4	0.722	0.067	0.15	Pred 50mg qd HCQ 0.2g bid MMF 0.5g bid

SLE-26	1	F	32	99	Rash, oral ulcer	8	3.59	199	320	74.3	0.739	0.214	0.06	Pred 10mg qd HCQ 0.2g bid MMF 0.75g bid
SLE-27	1	F	26	25	Proteinuria, arthritis, rash	10	8.92	207	320	17	1.470	0.272	1.79	Pred 12.5mg qd HCQ 0.2g bid CTX 0.6 q2w
SLE-28	2	F	53	10	Thrombocytopenia, arthritis,	9	8.5	60	80	33.5	0.913	0.120	0.06	Pred 10mg qd HCQ 0.2g bid
SLE-29	1	F	26	168	LN	20	4.3	168	640	436.82	0.502	0.094	1.4	Pred 50mg qd MMF 0.75g bid HCQ 0.2g bid
SLE-30	1	F	27	72	LN	12	13.33	280	640	42.4	1.220	0.197	1.44	Pred 30mg qd MMF 0.25g bid HCQ 0.2g bid
SLE-31	2	F	48	0.5	Arthritis, headache, thrombocytopenia, leucopenia	18	2.0	83	640	189.46	0.280	0.038	—	Pred 50mg qd MMF 0.5g bid HCQ 0.2g bid
SLE-32	2	F	31	42	Rash, Alopecia	8	6.2	282	640	436.34	0.667	0.062	0.06	Pred 7.5mg qd HCQ 0.2g bid
SLE-33	1	F	51	126	LN	10	4.45	199	80	342.68	0.807	0.191	0.36	Pred 5mg qd HCQ 0.2g bid LEF 20mg qd
SLE-34	2	F	31	1	Arthritis, alopecia, fever	11	11.2	208	640	84	0.627	0.102	0.1	Pred 45mg qd HCQ 0.2g bid CsA 25mg tid
SLE-35	2	F	21	49	Arthritis,	9	5.86	96	640	1.0	0.863	0.176	—	Pred 15mg qd

					rash, alopecia, thrombocytopenia,									HCQ 0.2g bid
SLE-36	1	F	24	3	Alopecia, LN	14	5.03	144	320	37.7	0.666	0.103	0.1	Pred 30mg qd HCQ 0.2g bid LEF 10mg bid
SLE-37	1	F	48	1	Alopecia, arthritis vasculitis, thrombocytopenia.	21	5.2	84	320	148.37	0.375	0.040	1.8	Pred 50mg qd HCQ 0.2 bid
SLE-38	2	F	28	32	Thrombocytopenia, alopecia, hematuria	11	13.82	4	640	103.4	0.284	0.025	—	Pred 50mg qd CsA 25mg bid HCQ 0.2 bid
SLE-39	2	F	41	8	Arthritis, rash	8	4.62	221	320	146.2	0.91	0.149	0.13	Pred 45mg qd HCQ 0.2 bid
SLE-40	1	M	34	4	Discoid rash，arthritis	8	4.34	233	320	43.9	1.030	0.211	0.16	MTX 10mg qw HCQ 0.2 bid
SLE-41	1	F	38	1	Vasculitis	12	6.5	221	320	465.78	0.447	0.127	0.33	Pred 50mg qd MMF 50mg bid HCQ 0.2g bid
SLE-42	1	F	27	40	Rash, alopecia	8	5.43	253	160	1.0	1.040	0.200	0.06	Pred 5mg qd HCQ 0.2g bid
SLE-43	2	F	25	204	LN	12	4.33	345	320	25.8	0.535	0.193	1.47	
SLE-44	2	F	20	5	LN	12	9.02	338	320	2525.53	0.563	0.017	0.27	Pred 15mg qd HCQ 0.2g bid MTX 10mg qw
SLE-45	2	F	23	46	Rash, arthritis	10	4.2	149	320	2460.8	0.563	0.017	0.05	Pred 10mg qd HCQ 0.2g bid

														MMF 0.25g tid
SLE-46	1	F	28	240	LN	12	6.3	202	640	32.8	0.781	0.225	7.36	Pred 10mg qd MMF 1.0g bid HCQ 0.2 bid
SLE-47	2	F	32	52	LN, rash	8	5.09	161	320	19.8	0.640	0.158	2.54	Pred 27.5mg qd HCQ 0.2g bid
SLE-48	1	F	37	40	Arthritis, alopecia ,LN	12	6.99	163	320	23.5	0.704	0.142	0.4	Pred 10mg qd HCQ 0.2g bid AZA 100mg qd
SLE-49	2	F	21	120	Alopecia, vasculitis	12	5.22	224	320	394.98	0.829	0.179	0.12	Pred 40mg qd HCQ 0.2g bid MMF 0.75g bid
SLE-50	2	F	25	56	Arthritis, myositis	12	6.39	162	320	73.3	0.767	0.103	0.11	Pred 10mg qd HCQ 0.2g bid
SLE-51	1	F	23	5	Alopecia, hematouria	10	8.77	267	160	29.6	0.720	0.104	0.19	Pred 20mg qd HCQ 0.2g bid
SLE-52	1	F	46	10	Arthritis, oral ulcers, thrombocytopenia	9	6.42	62	80	6.2	0.989	0.147	—	Pred 10mg qd HCQ 0.2g bid
SLE-53	1	M	18	30	Thrombocytopenia, rash, arthritis, alopecia	13	4.97	1	320	34.8	0.616	0.123	—	HCQ 0.2g bid
SLE-54	1	F	59	235	Thrombocytopenia, rash, LN	11	4.18	68	640	6.4	1.090	0.343	0.39	Pred 10mg qd HCQ 0.2g bid
SLE-55	2	F	30	50	LN, vasculitis	18	3.64	283	320	10.5	0.536	0.101	4.48	Pred 10mg qd HCQ 0.2g bid AZA 75mg qd

SLE-56	2	F	55	0	Arthritis, myositis, rash	12	12.56	256	40	44.3	1.140	0.225	0.37	Pred 15mg qd HCQ 0.2g bid
SLE-57	2	F	32	135	LN, alopecia, rash	10	8.02	110	320	119.8	0.922	0.268	0.64	Pred 10mg qd HCQ 0.2g bid MMF 0.5g bid
SLE-58	1	F	30	39	Vasculitis, alopecia	14	3.91	239	640	25.4	2.250	0.158	0.46	Pred 10mg qd HCQ 0.2 bid LEF 10mg bid
SLE-59	2	F	31	110	Headache, rash	12	3.8	159	80	1.0	0.564	0.056	0.3	Pred 50mg qd HCQ 0.2g bid MMF 0.5g bid
SLE-60	1	F	27	16	Alopecia, arthritis	8	4.87	196	320	15.5	0.789	0.129	0.06	Pred 10mg qd HCQ 0.2g bid

Table S3. Clinical responses to IL-2 or placebo treatment in patients with SLE

ID	Groups (1= IL-2 2= Placebo)	Clinical Responses	SLEDAI changes Pre and Post therapy	Response description	Description of adverse effects
SLE-1	1	Remission in proteinuria and rash	12-2=10	1. Rash resolved after week 6. 2. Renal variables: 24h-UPE decreased from 1.339 to 0.27 g/day after three courses of treatment. 3. Immune variables: anti-dsDNA antibodies decreased from 38.4 to 34.9 IU/mL, C3 increased from 0.794 to 0.863 g/L; C4 increased from 0.205 to 0.256 g/L after three courses of treatment.	Injection site reactions
SLE-2	2	Remission in fever Withdrew at week 16	13-8=5	1. Fever reduced to normal after week 2. 2. More swollen joints after treatment. 3. Immune variables: anti-dsDNA antibodies decreased from 132.1 to 47.7 IU/mL, C3 increased from 0.450 to 0.942 g/L; C4 increased from 0.05 to 0.149 g/L.	None
SLE-3	1	Remission in fever and NPSLE	27-14=13	1. Fever reduced to normal after week 2 and NPSLE was controlled after three courses of treatment. 2.More hurt joints and alopecia after three courses of treatment. 3. Renal variables: 24h-UPE increased from 0.09 to 0.47g/day; RBC increased from 10 to 1072/ml; serum albumin increased from 29.4 to 41.5g/L. 4.Immune variables: anti-dsDNA antibodies decreased from 260.4 to 111.1 IU/mL;	None

				anti-Rib-p antibodies decreased from 217.79 to 57.09 IU/mL; C3 increased from 0.307 to 0.681 g/L; C4 increased from 0.048 to 0.142 g/L after three courses of treatment.	
SLE-4	2	No remission in arthritis, rash and LN	14-14=0	1. More swollen/hurt joints and rash after three courses of treatment. 2.Renal variables: 24h-UPE increased from 1.22 to 2.87g/day; WBC increased from 0 to 89/□l; RBC decreased from 50 to 23/□l. 3. Immune variables: anti-dsDNA antibodies decreased from 321.4 to 124.6 IU/mL; C3 increased from 0.326 to 0.708 g/L; C4 increased from 0.034 to 0.101 g/L.	None
SLE-5	2	Partial remission in proteinuria	10-6=4	1.Renal variables: 24h-UPE decreased from 6.54 to 2.15g/day; RBC decreased from 72 to 2/□l; serum albumin changed from 35.4 to 40.1 g/L. 2.Immune variables: anti-dsDNA antibodies changed from 4.3 to 8.7 IU/mL; anti-Rib-p antibodies decreased from 217.79 to 57.09 IU/mL; C3 decreased from 0.711 to 0.625 g/L; C4 increased from 0.232 to 0.255 g/L.	Upper respiratory infection
SLE-6	1	Remission in arthritis, rash and alopecia Withdrew at week 16	12-4=8	1.Rash and arthritis resolved after 1 course; alopecia improved after week 8. 2. Immune variables: anti-dsDNA antibodies increased from 35.6 to 58.3 IU/mL; C3 increased from 0.672 to 0.787 g/L; C4 increased from 0.102 to 0.156 g/L after three courses of treatment.	None
SLE-7	2	Remission in arthritis and proteinuria	22-16=6	1. Arthritis relieved after week 16. 2. Renal variables: 24h-UPE decreased from 5.75 to 2.71g/day; WBC decreased from 433 to 50/□L; RBC changed from 104 to 104/□L serum albumin increased from 25.1 to 31.9 g/L.	None

				3. Immunevariables: anti-dsDNA antibodies decreased from 852.97 to 205.82 IU/mL; anti-Rib-p antibodies decreased from 36.73 to 15.03 IU/mL; C3 decreased from 0.421 to 0.478 g/L; C4 increased from 0.074 to 0.093 g/L.	
SLE-8	1	Remission in thrombocytopenia, arthritis and pericarditis	9-0=9	1. Pericarditis improved after week 6 and arthritis relieved after week 10. 2. PLT increased from 96 to 124×10^9/L. 3. Immune variables: anti-dsDNA antibodies changed from 14.9 to 16.2 IU/mL, C3 increased from 0.712 to 0.841 g/L; C4 increased from 0.164 to 0.179 g/L after three courses of treatment.	None
SLE-9	2	Remission in thrombocytopenia, fever, rash and arthritis	8-0=8	1. Rash disappeared and fever reduced to normal after week 2; arthritis relieved after week 8. 2. PLT increased from 76 to 135×10^7/ml after week 10. 3. Immune variables: anti-dsDNA antibodies changed from 20.2 to 19.9 IU/mL, C3 changed from 0.965 to 0.893 g/L; C4 increased from 0.184 to 0.202 g/L.	None
SLE-10	2	Withdrew at week 8	10-21=-11	1. Rash did not improved after treatment. 2. Developed to NPSLE and fever at week 8 3. Renal variables: 24h-UPE increased from 0.35 to 0.41g/day. 4.WBC decreased from 4.89 to 2.8×10^9/L; PLT decreased from 241 to 100×10^9/L.	NPSLE
SLE-11	1	Remission in proteinuria	16-16=0	1.Renal variables: 24h-UPE decreased from 2.14 to 1.02g/day; WBC decreased from 42 to 27/□L; RBC decreased from 21 to 25/□L;	None

				granular cast decreased from 10 to 6; serum albumin changed from 41.7 to 42.4 g/L after three courses of treatment. 2.Immune variables: anti-dsDNA antibodies changed from 2.6 to 6.8 IU/mL; C3 changed from 0.806 to 0.790 g/L; C4 changed from 0.416 to 0.289 g/L after three courses of treatment.	
SLE-12	1	Remission in arthritis, fever, rash, myositis	15-4=11	1. Fever reduced to normal after week 2; arthritis and myositis improved after week 8; rash disappeared after week 12. 2. Immune variables: anti-dsDNA antibodies changed from 60.7 to 59 IU/mL, C3 changed from 0.513 to 0.0.882 g/L; C4 increased from 0.080 to 0.139 g/L after three courses of treatment.	None
SLE-13	2	Remission in alopecia and arthritis	8-2=6	1. Alopecia resolved after week 2; arthritis relieved after week 6. 2. Immune variables: anti-dsDNA antibodies changed from 1 to 6.5 IU/mL, C3 increased from 0.718 to 0.842 g/L; C4 decreased from 0.169 to 0.148 g/L.	Herpes zoster
SLE-14	2	Remission in arthritis and oral ulcer	8-2=6	1. Oral ulcer recovered after week 4; arthritis relieved after week 6. 2. Immune variables: anti-dsDNA antibodies changed from 7.7 to 9.4 IU/mL, C3 changed from 0.928 to 1.040 g/L; C4 changed from 0.152 to 0.164 g/L.	None
SLE-15	1	Remission in vasculitis and oral ulcer	16-4=12	1. Oral ulcer recovered after week 2; fingertip vasculitis improved after week 6. 2. Immune variables: anti-dsDNA antibodies decreased from 162.8 to 36.45 IU/mL, anti-Rib-p antibodies decreased from 319.89 to 273.65 IU/mL; C3 changed from 0.836 to 0.985 g/L; C4 changed from 0.086 to 0.108 g/L after three courses of treatment.	Injection site reactions

SLE-16	1	Withdrew at week 2	—	Without using study drug.	
SLE-17	2	Remission in thrombocytopenia and rash, no remission in proteinuria	15-12=3	1. Rash resolved after week 4. 2. PLT increased from 93 to 167×10^9/L. 3.Renal variables: 24h-UPE increased from 2.61 to 4.98g/day; WBC decreased from 48 to 33/□L; serum albumin decreased from 41.5 to 37.6g/L. 4. Immune variables: anti-dsDNA antibodies decreased from 164 to 80.9 IU/mL; C3 decreased from 0.514 to 0.553 g/L; C4 decreased from 0.074 to 0.060 g/L.	None
SLE-18	1	Remission in rash, alopecia and arthritis	10-4=6	1. Arthritis relieved after week 2; rash and alopecia improved after week 4. 2. Immune variables: anti-dsDNA antibodies increased from 22.6 to 31.4 IU/mL; C3 increased from 0.701 to 0.765 g/L; C4 increased from 0.157 to 0.177 g/L after three courses of treatment.	Flu-like symptoms
SLE-19	2	Remission in proteinuria and rash	8-6=2	1. Rash resolved after week 2. 2. Renal variables: 24h-UPE decreased from 1.42 to 1.38g/day. 3. Immune variables: anti-dsDNA antibodies decreased from 46 to 27.6 IU/mL; C3 changed from 1.250 to 1.020 g/L; C4 changed from 0.208 to 0.161 g/L.	Injection site reactions; Upper respiratory infection
SLE-20	1	Remissive in proteinuria	12-12=0	1. Renal variables: 24h-UPE decreased from 1.80 to 1.33g/day; WBC changed from 32 to 43/□L after three courses of treatment. 3. Immune variables: anti-dsDNA antibodies decreased from 1783.15 to 876.21 IU/mL; C3 decreased from 0.735 to 0.477 g/L; C4 changed from 0.092 to 0.055 g/L after three courses of treatment.	Flu-like symptoms

SLE-21	2	No remission in proteinuria	12-12=0	1. Renal variables: 24h-UPE increased from 1.63g/day to 7.89g/day; WBC changed from 70 to 432/□L. 3. Immune variables: anti-dsDNA antibodies decreased from 129.2 to 50.2 IU/mL; C3 increased from 0.431 to 0.649 g/L; C4 increased from 0.106 to 0.134 g/L.	None
SLE-22	1	Remission in rash, fever, thrombocytopenia and leukopenia	9-4=5	1. Fever reduced to normal after week 2; rash disappeared after week 4. 2. Hematological variables: WBC increased from 1.7 to 6.67×10^9/ml; PLT increased from 58 to 102×10^9/ml after one course of treatment. 3. Immune variables: anti-dsDNA antibodies increased from 30.9 to 37.8 IU/mL; C3 changed from 1.02 to 0.847 g/L; C4 decreased from 0.153 to 0.147 g/L after three courses of treatment.	Upper respiratory infection
SLE-23	2	Remission in arthritis Withdrew at week 12	11-4=7	1. Arthritis relieved after week 6. 2. Hematological variables: WBC increased from 2.89 to 3.67×10^9/ml. 3. Immune variables: anti-dsDNA antibodies increased from 58.5 to 37.6 IU/mL; C3 changed from 0.502 to 0.872 g/L; C4 decreased from 0.094 to 0.137 g/L after three courses of treatment.	None
SLE-24	1	Remission in proteinuria, arthritis and rash	16-4=12	1. Remission of arthritis and rash after week 2, remission of proteinuria after week 24. 2. Renal variables: 24h-UPE decreased from 1.17 to 0.38g/day; RBC changed from 102 to 20/□L. after week 24. 3. Immune variables: anti-dsDNA antibodies decreased from 28.4 to 15.3 IU/mL; C3	Injection site reactions; Upper respiratory infection

				changed from 1.080 to 1.160 g/L; C4 changed from 0.163 to 0.163 g/L after three courses of treatment.	
SLE-25	2	Remission in rash and fever	8-4=4	1. Rash improved and fever reduced to normal after week 2. 2. Hematological variables: PLT increased from 118 to 267×10^9/ml. 3. Immune variables: anti-dsDNA antibodies decreased from 37.4 to 3.6 IU/mL; C3 increased from 0.722 to 0.885 g/L; C4 changed from 0.067 to 0.180 g/L.	Pneumonia
SLE-26	1	Remission in rash and oral ulcer	8-4=4	1. Rash and oral ulcer improved after week 4. 2.Immune variables: anti-dsDNA antibodies decreased from 74.3 to 57.8 IU/mL; C3 increased from 0.739 to 0.520 g/L; C4 increased from 0.214 to 0.189 g/L after three courses of treatment.	Injection site reactions
SLE-27	1	Remission in rash	10-8=2	1. Rash disappeared after week 2. 2. Renal variables: 24h-UPE changed from 1.79 to 1.66g/day after three courses of treatment. 3. Immune variables: anti-dsDNA antibodies changed from 17 to 13.4 IU/mL; C3 changed from 1.470 to 1.620 g/L; C4 changed from 0.272 to 0.352 g/L after three courses of treatment.	Injection site reactions; Transient fever
SLE-28	2	Withdrew at week 2	—		
SLE-29	1	Remission in proteinuria	20-4=16	1. Renal variables: 24h-UPE changed from 1.40 to 3.03g/day; WBC decrseased from 119 to 9/□L; WBC changed from 34 to 10/□L; cylindruria 6 to 0 serum albumin increased from 34.9 to 46.9g/L after three courses of treatment.	Injection site reactions

				2. Immune variables: anti-dsDNA antibodies decreased from 436.82 to 36.4 IU/mL; C3 increased from 0.502 to 0.776 g/L; C4 increased from 0.094 to 0.180 g/L after three courses of treatment.	
SLE-30	1	Remission in proteinuria	12-8=4	1. Renal variables: 24h-UPE changed from 1.44 to 0.84g/day after three courses of treatment. 2. Immune variables: anti-dsDNA antibodies decreased from 42.4 to 7 IU/mL; anti-Rib-p antibodies decreased from 23.12 to 0.57 IU/ml; C3 changed from 1.22 to 1.530 g/L; C4 increased from 0.197 to 0.317 g/L after three courses of treatment.	None
SLE-31	2	Remission in arthritis, thrombocytopenia and leukopenia	18-2=16	1.Arthritis relieved after week 2. 2. Hematological variables: WBC increased from 2.0 to 4.08×10^9/ml after week 8; PLT increased from 83 to 231×10^9/ml after week 8. 2. Immune variables: anti-dsDNA antibodies decreased from 189.46 to 23 IU/mL; C3 increased from 0.280 to 0.710 g/L; C4 increased from 0.038 to 0.126 g/L.	None
SLE-32	2	Remission in rash and alopecia	8-4=4	1. Rash and alopecia resolved after week 12. 2. Immune variables: anti-dsDNA antibodies decreased from 436.34 to 146.5 IU/mL; C3 increased from 0.667 to 0.838 g/L; C4 increased from 0.062 to 0.107 g/L.	Injection site reactions; Upper respiratory infection
SLE-33	1	Remission in proteinuria	10-4=6	1. Renal variables: 24h-UPE changed from 0.36 to 0.28g/day after week 24; RBC decreased from 147 to 12/□L. 2. Immune variables: anti-dsDNA antibodies decreased from 342.68 to 149.7 IU/mL; C3	Fatigue

				changed from 0.807 to 0.738 g/L; C4 changed from 0.191 to 0.197 g/L after three courses of treatment.	
SLE-34	2	Remission in alopecia and fever	11-6=5	1. Fever reduced to normal and alopecia improved after week 2. 2. Immune variables: anti-dsDNA antibodies decreased from 84.0 to 13.2 IU/mL; C3 changed from 0.627 to 0.836 g/L; C4 changed from 0.102 to 0.129 g/L.	None
SLE-35	2	Remission in rash and thrombocytopenia	9-4=5	1. Rash resolved after week 4. 2. PLT increased from 96 to 153×10^9/ml after week 8. 3. Immune variables: anti-dsDNA antibodies changed from 1 to 1 IU/mL; C3 changed from 0.863 to 0.943 g/L; C4 changed from 0.176 to 0.185 g/L.	None
SLE-36	1	Remission in leucocyturia	14-4=10	1. Renal variables: WBC decreased from 51 to 16/□L after three courses of treatment. 3. Immune variables: anti-dsDNA antibodies changed from 37.7 to 33 IU/mL; C3 increased from 0.666 to 0.708 g/L; C4 increased from 0.103 to 0.145 g/L after three courses of treatment.	None
SLE-37	1	Remission in alopecia, arthritis, vasculitis and thrombocytopenia	21-8=13	1. Vasculitis improved after week 4; alopecia and arthritis resolved after three courses of treatment. 2. PLT increased from 84 to 207×10^9/ml after week 24; 3. Immune variables: anti-dsDNA antibodies changed from 148.37 to 60.7 IU/mL; C3 increased from 0.375 to 0.855 g/L; C4 increased from 0.040 to 0.138 g/L after three courses of treatment.	None

SLE-38	2	Remission in alopecia, thrombocytopenia and hematouria	11-4=7	1. Alopecia improved after week 6. 2. Hematological variables: PLT increased from 4.0 to 79×10^7/ml after week 24. 3. Immune variables: anti-dsDNA antibodies changed from 103.4 to 41.5 IU/mL; C3 increased from 0.284 to 0.761 g/L; C4 increased from 0.025 to 0.133 g/L.	None
SLE-39	2	Withdrew at week 4	—		
SLE-40	1	Remission in arthritis	8-2=6	1. Arthritis relieved after week 2. 2. Immune variables: anti-dsDNA antibodies changed from 43.9 to 66.2 IU/mL; C3 changed from 1.030 to 1.220 g/L; C4 changed from 0.211 to 0.231 g/L after three courses of treatment.	Transient fever
SLE-41	1	Remission in vasculitis	12-6=6	1. Lupus mesenteric vasculitis improved after week 2. 2. Immune variables: anti-dsDNA antibodies changed from 465.78 to 51.8 IU/mL; C3 increased from 0.447 to 0.697 g/L; C4 increased from 0.127 to 0.152 g/L after three courses of treatment.	None
SLE-42	1	Remission in alopecia and rash	8-0=8	1. Alopecia and rash resovled after week 4. 2. Immune variables: anti-dsDNA antibodies changed from 1 to 1 IU/mL; C3 changed from 1.040 to 0.993 g/L; C4 changed from 0.200 to 0.197 g/L after three courses of treatment.	Injection site reactions
SLE-43	2	Remission in proteinuria	12-8=4	1. Renal variables: 24h-UPE decreased from 1.47 to 0.81 g/day. 2. Immune variables: anti-dsDNA antibodies changed from 25.8 to 39.8 IU/mL; C3 increased from 0.535 to 0.621 g/L; C4 changed from 0.193 to 0.252	None

				g/L.	
SLE-44	2	No remission in proteinuria	12-8=4	1. Renal variables: 24h-UPE increased from 0.27 to 0.35 g/day after treatment. 2. Immune variables: anti-dsDNA antibodies increased from 2525.53 to 3467.8 IU/mL; C3 increased from 0.563 to 0.594 g/L; C4 changed from 0.017 to 0.107 g/L.	None
SLE-45	2	Remission in rash and arthritis	10-4=6	1. Rash resolved after week 2; arthritis relieved after week 8. 2. Immune variables: anti-dsDNA antibodies changed from 2460.8 to 173.6 IU/mL; C3 decreased from 0.586 to 0.541 g/L; C4 changed from 0.101 to 0.103 g/L.	None
SLE-46	1	Remission in proteinuria Withdrew at week 12	12-10=2	1. Renal variables: 24h-UPE increased from 7.36 to 3.57 g/day after treatment. 2. Immune variables: anti-dsDNA antibodies decreased from 32.8 to 17.4 IU/ml; C3 increased from 0.781 to 0.796 g/L; C4 changed from 0.225 to 0.24 g/L after three courses of treatment.	None
SLE-47	2	Remission in rash and proteinuria	8-6=2	1. Rash resolved after week 2. 2.Renal variables: 24h-UPE decreased from 2.54 to 1.18 g/day. 3. Immune variables: anti-dsDNA antibodies changed from 19.8 to 17.8 IU/mL; C3 decreased from 0.640 to 0.593 g/L; C4 increased from 0.158 to 0.188 g/L.	None
SLE-48	1	Remission in arthritis and alopecia	12-2=10	1. Arthritis and alopecia improved after week 6. 2. Immune variables: anti-dsDNA antibodies changed from 23.5 to 11 IU/mL; C3 increased	Injection site reactions

				from 0.704 to 0.770 g/L; C4 increased from 0.142 to 0.176 g/L after three courses of treatment.	
SLE-49	2	Remission in alopecia and vasculitis	12-6=6	1.Vasculitis and alopecia improved after week 6. 2. Immune variables: anti-dsDNA antibodies decreased from 394.98 to 54.5 IU/mL; C3 decreased from 0.829 to 0.761 g/L; C4 changed from 0.179 to 0.216 g/L.	Upper respiratory infection (Pharyngitis)
SLE-50	2	Remission in myositis	12-4=8	1. Myositis improved after week 4; arthritis relieved after week 24. 2. Immune variables: anti-dsDNA antibodies increased from 73.3 to 117.8 IU/mL; C3 decreased from 0.767 to 0.551 g/L; C4 decreased from 0.103 to 0.078 g/L.	None
SLE-51	1	Remission in hematouria	10-8=2	1. Renal variables: RBC decreased from 250 to 4/□L; WBC decreased from 24 to 6/□L after three courses of treatment. 2. Immune variables: anti-dsDNA antibodies changed from 29.6 to 31.9 IU/mL; C3 decreased from 0.72 to 0.633 g/L; C4 increased from 0.104 to 0.117 g/L after three courses of treatment.	Flu-like symptoms
SLE-52	1	Remission in arthritis and oral ulcers	9-5=4	1. Oral ulcers improved after week 4; arthritis relieved after week 6. 2. Hematological variables: PLT increased from 62 to 83×10^9/ml after three courses of treatment. 3. Immune variables: anti-dsDNA antibodies changed from 6.2 to 11.1 IU/mL; C3 changed from 0.989 to 0.870 g/L; C4 increased from 0.147 to 0.166 g/L after three courses of treatment.	Injection site reactions
SLE-53	1	Remission in rash, alopecia and arthritis	13-7=6	1. Alopecia and rash improved after week 2; arthritis relieved after week 4.	None

				2. Hematological variables: PLT increased from 70 to 102×10^9/ml after three course of treatment. 3. Immune variables: anti-dsDNA antibodies changed from 34.8 to 26.6 IU/mL; C3 increased from 0.616 to 0.668 g/L; C4 increased from 0.123 to 0.187 g/L after three courses of treatment.	
SLE-54	1	Remission in rash and proteinuria	11-9=2	1. Rash improved after week 2. 2. Renal variables: 24h-UPE decreased from 0.39 to 0.28 g/day after two courses of treatment. 3. Hematological variables: PLT increased from 68 to 100×10^9/ml after two courses of treatment, but decreased to 60×10^9/ml after three courses of treatment. 4. Immune variables: anti-dsDNA antibodies changed from 6.4 to 10.8 IU/mL; C3 changed from 1.090 to 1.520 g/L; C4 changed from 0.343 to 0.417 g/L after three courses of treatment.	Transient fever
SLE-55	2	Remission in vasculitis	18-12=6	1. Vasculitis improved after week 10. 2. Renal variables: 24h-UPE increased from 4.48 to 5.48 g/day; serum albumin decreased from 35.3 to 33.8 g/day. 4. Immune variables: anti-dsDNA antibodies increased from 10.5 to 34.6 IU/mL; C3 changed from 0.536 to 0.576 g/L; C4 changed from 0.101 to 0.101 g/L.	None
SLE-56	2	Remission in arthritis and myositis	12-6=6	1. Arthritis and myositis improved after week 20. 2. Immune variables: anti-dsDNA antibodies decreased from 44.3 to 37 IU/mL; C3 decreased from 1.140 to 0.946 g/L; C4 changed from 0.225 to 0.200	Urinary tract infection

				g/L.	
SLE-57	2	Remission in rash and proteinuria	10-3=7	1. Rash improved after week 2. 2. Renal variables: 24h-UPE decreased from 0.64 to 0.38 g/day. 3. Immune variables: anti-dsDNA antibodies increased from 119.8 to 173.2 IU/mL; C3 changed from 0.922 to 0.808 g/L; C4 changed from 0.268 to 0.300 g/L.	None
SLE-58	1	Remission in vasculitis and alopecia	14-6=8	1. Alopecia improved after week 4; vasculitis improved after week 10. 2. Immune variables: anti-dsDNA antibodies increased from 25.4 to 43.5 IU/mL; C3 changed from 1.250 to 0.909 g/L; C4 changed from 0.158 to 0.151 g/L after three courses of treatment.	None
SLE-59	2	Remission in rash	12-2=10	1. Rash improved after week 2. 2. Immune variables: anti-dsDNA antibodies increased from 1 to 7.2 IU/mL; C3 increased from 0.564 to 0.912 g/L; C4 increased from 0.056 to 0.222 g/L.	None
SLE-60	1	No remission in alopecia and arthritis	8-10=-2	1. Immune variables: anti-dsDNA antibodies increased from 15.5 to 28.8 IU/mL; C3 changed from 0.789 to 0.764 g/L; C4 changed from 0.129 to 0.143 g/L after three courses of treatment.	Transient fever

Table S4. Responses of SLE patients to low-dose IL-2 treatment

Characteristics	Baseline	Week 12	Week 24	week 0 vs 12 vs 24	IL-2 vs placebo
SLEDAI, median (range)					
IL-2	12 (8-27)	6 (0-16)[aa]	4 (0-18)[aa]	*F*=18.561,	*F*=0.251,
Placebo	11 (8-22)	6 (0-25)[aa]	8 (0-25)[a]	*P*<0.001	*P*=0.628
≥1 BLIAG A or 2B score,% (%)					
IL-2	21 (72.41)	2 (6.9)	1 (3.45)	*X^2=0.843,*	
Placebo	21 (70)	4 (13.33)	2 (6.67)	*P=0.656*	
PGA, median (range)					
IL-2	2.3 (1.55-2.75)	0 (0-2) [aaa]	0 (0-1) [aaab]	*F*=54.898,	*F*=2.705,
Placebo	2.2 (1-2.3)	1 (0-2) [aaa]	1 (0-1) [aa]	*P*<0.001	*P*=0.112
Rash, n (%)					
IL-2	13 (44.83)	2 (6.90)	2 (6.90)	*X^2=1.781,*	
Placebo	16 (53.33)	6 (20.0)	6 (20.0)	*P=0.411*	
Oral ulceration, n (%)					
IL-2	4 (13.79)	0 (0)	0 (0)	-	
Placebo	1 (3.33)	0 (0)	0 (0)		
Arthritis, n (%)					
IL-2	14 (48.28)	4 (13.79)	3 (10.34)	*X^2=2.067,*	
Placebo	15 (50.0)	9 (30.00)	8 (26.67)	*P=0.356*	
Vasculitis, n (%)					
IL-2	4 (13.79)	0 (0)	0 (0)	-	
Placebo	2 (6.67)	0 (0)	0 (0)		
Alopecia, n (%)					
IL-2	12 (41.38)	6 (20.69)	5 (17.24)	*X^2=0.425,*	
Placebo	7 (23.33)	2 (6.67)	2 (6.67)	*P=0.809*	
Fever, n (%)					
IL-2	3 (10.34)	0 (0)	0 (0)	*X^2*=0.024,	
Placebo	4 (13.33)	1 (3.33)	0 (0)	*P*=0.312	
Myositis, n (%)					
IL-2	1 (3.45)	0 (0)	0 (0)	-	
Placebo	2 (6.67)	0 (0)	0 (0)		
Prednisone dose, mg/day, median (range)					
IL-2	15 (0-50)	10 (0-25)[aa]	10 (0-20)[aa]	*F*=13.872,	*F*=0.232,
Placebo	15 (7.5-60)	15 (5-40)	10 (2.5-35)[a]	*P<0.001*	*P*=0.634
ANA decreased, n (%)					
IL-2, n=29	0 (0)	7 (24.14)	8 (27.59)	*X^2*=0.005,	

Placebo, n=30	0 (0)	11 (36.67)	12(40.0)	*P*=0.944	
Anti-ds-DNA, IU/ml, median (range)					
IL-2, n=29	34.80 (1.0-1783.15)	33.0 (7.0-876.21)	29.0 1.0-348.50)	*F*=8.955, *P*=0.005	*F*=0.067, *P*=0.807
Placebo, n=30	73.30 (1.0-2525.53)	37.60 (1.40-3467.80)	36.3 (1.0-3467.80)		
AnuA, IU/ml, median (range)					
IL-2, n=29	14.45 (0.87-449.06)	20.84 (1.28-287.07)	16.72 (1.17-287.07)	*F*=1.358, *P*=0.451	*F*=1.323, *P*=0.456
Placebo, n=30	41.725 (0.0-315.80)	16.03 (0.0-296.32)	12.08 (0.0-266.740)		
Albumin, g/L, median (range)					
IL-2, n=29	39.25 (27.60,44.70)	43.90 (37.70,46.90)	43.50 (39.80,47.20)	*F*=1.282, *P*=0.276	*F*=0.141, *P*=0.302
Placebo, n=30	39.80 (25.10,44.40)	38.65 (31.90,43.60)	40.40 (32.80,47.50)		
LN Complete remission, n (%)					
IL-2, n=13	0 (0)	7 (53.85)	7 (53.85)	X^2=0.281,	
Placebo, n=12	0 (0)	1 (8.33)	2 (16.67)	*P*=0.596	
LN Partial remission, n (%)					
IL-2, n=13	0 (0)	10 (76.92)	10 (76.92)	X^2=0.708,	
Placebo, n=12	0 (0)	3 (25.0)	6 (50.0)	*P*=0.400	

[a] means $\alpha<0.05$, [aa] means $\alpha<0.01$, compared to Baseline

[b] means $\alpha<0.05$, compared to week 12

Table S5 Laboratory Improvement in LN patients

Variable	12 Weeks of Treatment		24 Weeks of Treatment	
	IL-2 (n=13)	Placebo (n=12)	IL-2 (n=13)	Placebo (n=12)
PRO，g/24hr	0.78 (0.06,2.39)	1.765 (0.17,5.48)*	0.48 (0.06,1.42)	1.08 (0.26,7.75) *
Alb, g/L	43.90 (37.70,46.90)	38.65 (31.90,43.60)*	43.50 (39.80,47.20)	40.40 (32.80,47.50)
Cr，μmol/L	53.5 (43,298)	64.5 (40,138)	57 (45,129)	65 (40,109)
Routine urianlysis				
WBC, /μl	2（2,357）	11 (4,89)	11 (2,57)	10 (3,195)
RBC, /μl,	11 (3,241)	18 (2,104)	20.5 (2,317)	27.5 (9,166)
casts,n(%)	2 (15.38)	3 (25)	0 (0)	0 (0)
C3, mg/L	0.855 (0.70, 1.62)	0.623 (0.54, 1.02)	0.737 (0.64, 1.83)	0.769 (0.47, 1.20)
C4, mg/L	0.1800 (0.14, 0.42)	0.1745 (0.06, 0.30)	0.2270 (0.10,0.42)	0.1955 (0.09, 0.30)
Anti-dsDNA,IU/ml	22.25 (1.00,53.20)	59.85 (1.00,200.91)	27.35 (9.00,62.80)	35.70 (8.70,398.25)

(*:P<0.05)

Table S6. Viral load in SLE with IL-2 treatment

	Week 0	Week 2	Week10
BK virus	10^8 copy/ml	10^3 copy/ml	$<10^3$ copy/ml
BK virus	10^7 copy/ml	10^5 copy/ml	$<10^3$ copy/ml
HPV	++	N/A	—

He J, *et al. Ann Rheum Dis* 2019; 0:1–9. doi: 10.1136/annrheumdis-2019-215396

Table S7. Virus examined in sera of SLE patients by real-time PCR

No.	Virus	Normal values
1	Influenza A virus – H1N1	$<1.0\times10^3$ PFU/ml
2	Influenza B virus	$<1.5\times10^2$ PFU/ml
3	Influenza A virus	$<1.6\times10^2$ PFU/ml
4	Parainfluenza virus	$<1.0\times10^3$ copies/ml
5	Coxsackie virus	<CCID standard: 1.0×10^{-2}CCID50/0.1ml; plaque calculate: 1.0×10^3 PFU/ml
6	Mycoplasma pneumoniae	$<1.0\times10^4$ copies/ml
7	Legionella pneumophilia	$<1.0\times10^3$ copies/ml
8	Respiratory syncytial virus	$<1.0\times10^3$ copies/ml
9	Human bocavirus	$<1.0\times10^3$ copies/ml
10	Human metapneumovirus	$<1.0\times10^3$ copies/ml
11	Human coronavirus - 229E	$<1.0\times10^3$ copies/ml
12	Human coronavirus - HKU1	$<1.0\times10^3$ copies/ml
13	Human coronavirus - NL63	$<1.0\times10^3$ copies/ml
14	Human coronavirus - 229E	$<1.0\times10^3$ copies/ml
15	Herpes simplex virus	$<5.0\times10^3$ copies/ml
16	Human herpes virus-6	$<4.0\times10^2$ copies/ml
17	Human herpes virus-8	$<5.0\times10^3$ copies/ml
18	Enterovirus	<CCID standard: 5.0×10^2 $CCID_{50}$/0.1ml; Plaque calculate: 2.0×10^3 PFU/ml
19	Norwalk virus	$<1.0\times10^3$ copies/ml
20	Enterovirus-71	$<1.0\times10^3$ copies/ml
21	Rotavirus	$<1.0\times10^3$ copies/ml
22	BKV	$<5.0\times10^3$ copies/ml
23	JC virus	$<1.0\times10^3$ copies/ml
24	Adenoviridae	$<1.0\times10^4$ copies/ml
25	Cytomegalovirus	$<1.0\times10^3$ copies/ml
26	Varicella Zoster Virus	$<1.0\times10^3$ copies/ml
27	Mycobacterium	$<10^2$ Bacteria / PCR reaction
28	Human coronavirus -OC43	$<1.0\times10^4$ copies/ml
29	Epstein-Barr Virus	$<5.0\times10^3$ copies/ml
30	Human Parovirus B19	$<1.0\times10^3$ copies/ml

Table S8. Antibodies used in flow cytometric analysis in this study

Target antigen	Clone	Fluorochrome	Vendor
CD3	OKT3	Alexa Fluor 700	Biolegend
CD4	SK3	FITC	Biolegend
CD8	SK1	PerCP	Biolegend
CD25	BC96	PE	Biolegend
CD127	A019D5	Brilliant Violet 605	Biolegend
CD45RA	HI100	Brilliant Violet 510	Biolegend
CXCR3	G025H7	PECF 594	BD
CXCR5	J252D4	Alexa Fluor 647	BD
CCR6	G034E3	Brilliant Violet 650	Biolegend
CCR7	G043H7	Brilliant Violet 421	Biolegend
PD-1	EH12_2H7	PE-Cy7	Biolegend
CD56	HCD56	APC	eBiosense
CD16	3G8	Brilliant Violet 421	Biolegend

Table S9. Immune cell changes in SLE patients with low-dose IL-2 treatment

Variables	Baseline	Week 10	Week 12	Week 24	P value (Week 0 vs 10)	P value (Week 0 vs 12)
CD4+ T cells (%)						
IL-2, mean□SD	43.37±11.19	41.27±11.56	43.82±14.70	42.70±12.93	0.220	0.387
Placebo, mean□SD	41.61±11.24	40.68±11.61	45.02±10.35	39.97±14.76	0. 403	0.085
Treg cells (%)						
IL-2, mean□SD	12.77±10.25	16.79±8.60	14.19±6.07	12.11±6.27	0.007	0.020
Placebo, mean□SD	11.02±3.51	10.51±3.79	10.97±4.59	11.16±4.69	0.534	0.814
CD8+ T cells (%)						
IL-2, mean□SD	46.17±12.37	47.54±13.06	46.42±13.68	46.19±12.06	0.580	0.677
Placebo, mean□SD	45.78±13.83	46.07±14.85	45.16±13.20	49.62±14.18	0.931	0.905
NK cells (%)						
IL-2, mean□SD	6.48±4.85	12.07±8.01	10.2±8.05	7.28±4.15	0.003	0.012
Placebo, mean□SD	6.49±6.02	6.80±6.42	5.44±4.47	6.30±5.31	0.967	0.516
CD56bri in NK cells (%)						
IL-2, mean□SD	6.68±4.45	10.40±6.49	6.54±4.07	6.70±5.46	0.011	0.938
Placebo, mean□SD	8.10±6.99	6.56±4.65	7.43±5.67	9.41±7.53	0.476	0.737
CD56dim inNK cells (%)						
IL-2, mean□SD	76.20±9.47	68.27±17.5	78.77±9.48	78.22±9.21	0.059	0.423
Placebo, mean□SD	66.41±21.7	71.1±17.96	69.87±19.78	66.78±21.25	0.421	0.627

Table S10. Baseline characteristics of SLE patients in trial NCT02932137 (n=20)

Characteristics	IL-2 (n=10)	Placebo (n=10)	P value
Age, year, mean ±SD	35.2±11.76	32.9±11.96	0.670
Female/Male	9/1	10/0	1.000
Duration, year, mean ±SD	74.8±45.2	66.0±49.4	0.683
SLEDAI, median (range)	8.6±4.6	9.4±8.0	0.787
Medications			
Prednisone dose, mg/day, median (range)	15.13±10.35	17.75±20.19	0.719
Hydroxychloroquine	9 (90.0)	8 (80.0)	1.000
Cyclophosphamide	1 (10.0)	2 (20.0)	1.000
Cyclosporine	3 (30.0)	2 (20.0)	1.000
Mycophenolate Mofetil	4 (40.0)	2 (20.0)	0.626

Table S11. Phenotypic change of NK cells in SLE patients

Variables	Baseline	Post Treatment	P value
IFN-γ^+ NK cells (%)			
IL-2, mean±SD	68.92±16.92	82.81±12.22	0.024
Standard treatment, mean±SD	65.76±14.46	73.51±17.26	0.254
NKp46$^+$ NK cells (%)			
IL-2, mean±SD	92.68±4.40	96.87±2.71	0.025
Standard treatment, mean±SD	92.11±6.56	94.07±6.85	0.562
NKG2D$^+$ NK cells (%)			
IL-2, mean±SD	83.84±4.47	91.11±6.14	0.003
Standard treatment, mean±SD	88.46±6.18	88.02±6.92	0.748

* IL-2 group (n=10); standard treatment group (n=10).

Table S12. Phenotype changes of CD8+ T cells in SLE patients

Variables	Baseline	Post Treatment	P value
IFN-γ+ CD8+ T cells (%)			
IL-2, mean±SD	82.30±8.48	85.42±15.57	0.540
Standard treatment, mean±SD	74.29±12.89	77.87±15.06	0.553
TNF-□+ CD8+ T cells (%)			
IL-2, mean±SD	1.43±1.85	1.53±1.73	0.464
Standard treatment, mean±SD	2.03±3.05	2.35±3.21	0.493
Perforin+ CD8+ T cells (%)			
IL-2, mean±SD	10.07±6.27	8.46±5.57	0.248
Standard treatment, mean±SD	12.54±18.56	17.14±17.74	0.242

*IL-2 group (n=10); standard treatment group (n=10).

Table S13. SRI-4 changes in SLE patients

SRI-4 (%)	Week0	Week2	Week4	Week6	Week8	Week10	Week12	Week16	Week20	Week24
IL-2	0	10.34	17.24	34.48	37.93	48.28	55.17	58.62	65.52	65.52
Placebo	0	6.67	6.67	10.0	13.33	23.33	30.0	30.0	30.0	36.67
P value	-	0.968	0.394	0.023	0.030	0.045	0.052	0.027	0.06	0.027

Table S14. SLEDAI score changes in SLE patients

SLEDAI, median (range)	Week0	Week2	Week4	Week6	Week8	Week10	Week12	Week16	Week20	Week24
IL-2	12 (8-27)	8 (2-20)	7 (1-18)	6 (0-16)	6 (0-16)	4 (0-12)	6 (0-16)	4 (0-12)	4 (0-18)	4 (0-18)
Placebo	11 (8-22)	8 (0-20)	8 (0-20)	8 (0-16)	6 (0-25)	6 (2-25)	6 (0-25)	6 (0-25)	7 (0-25)	8 (0-25)
P value	0.378	0.921	0.192	0.290	0.198	0.052	0.618	0.177	0.013	0.027

Table S15. LN complete remission rates in SLE patients

LN Complete remission, n（%）	Week 0	Week 12	Week 24
IL-2, n=13	0 (0)	7 (53.85)	7 (53.85)
Placebo, n=12	0 (0)	1 (8.33)	2 (16.67)
P value	1.000	0.013	0.036

Table S16. Proportions of patients achieving corticosteroid reduction by ≥50% from baseline to 24 weeks

（%）	Week0	Week2	Week4	Week6	Week8	Week10	Week12	Week16	Week20	Week24
IL-2	0	0	0	3.45	6.90	24.14	37.93	41.38	44.83	44.83
Placebo	0	0	0	0	3.33	13.33	20.0	30.0	30.0	33.33
P value	-	-	-	0.492	0.487	0.233	0.109	0.261	0.182	0.262

Table S17. Changes of Albumin in SLE patients

Albumin, g/L, median (range)	Week 0	Week 12	Week 24	P value (Week 0 vs 12)	P value (Week 0 vs 24)
IL-2, n=13	40.50 (25.10,44.40)	38.30 (31.90,43.60)	40.40 (32.80,47.50)	0.386	0.293
Placebo, n=12	39.25 (27.60,44.70)	43.90 (37.70,46.90)	43.50 (39.80,47.20)	0.013	0.006
P value	0.712	0.002	0.186	--	--

Table S18. Changes of proteinuria per 24 hours in SLE patients

PRO，g/24hr	Week 0	Week 12	Week 24	P value (Week 0 vs 12)	P value (Week 0 vs 24)
IL-2, n=13	1.55±1.87	0.79±0.75	0.48±0.47	0.058	0.002
Placebo, n=12	2.42±2.09	2.21±1.83	3.44±2.68	0.466	0.372
P value	0.283	0.023	0.002	--	--

Table S19. Proportions of patients with recovered C3 levels from baseline to 24 weeks

（%）	Week0	Week2	Week4	Week6	Week8	Week10	Week12	Week16	Week20	Week24
IL-2	0	31.25	43.75	50	31.25	56.25	25	25	31.25	31.25
Placebo	0	15	28.57	38.10	38.10	42.86	33.33	28.57	23.81	23.81
P value	-	0.223	0.270	0.348	0.468	0.317	0.429	0.550	0.445	0.445

Table S20. Proportions of patients with recovered C4 levels from baseline to 24 weeks

（%）	Week 0	Week2	Week4	Week6	Week8	Week10	Week12	Week16	Week20	Week24
IL-2	0	11.76	5.885	35.29	17.65	47.06	29.41	41.18	41.18	35.29
Placebo	0	15	10	15	20	15	20	20	201	20
P value	-	0.580	0.562	0.147	0.420	0.038	0.140	0.034	0.034	0.072

Table S21. Changes of immune cell subsets

Variables	Baseline	Week 2	Week 4	Week 6	Week 8	Week 10	Week 12	Week 16	Week 20	Week 24
CD4+ T cells (%)										
IL-2, mean□SD	43.37±11.19	46.15±11.13	40.19±12.35	41.86±10.75	39.38±11.56	41.27±11.56	43.82±14.70	46.19±13.42	41.97±14.59	42.70±12.93
Placebo, mean□SD	41.61±11.24	40.70±13.64	41.20±12.43	39.11±13.68	40.16±12.25	40.68±11.61	45.02±10.35	44.72±9.14	43.06±10.40	39.97±14.76
P value	0.689	0.138	0.742	0.410	0.775	0.942	0.461	0.848	0.800	0.661
Treg cells (%)										
IL-2, mean□SD	12.77±10.25	17.62±8.37	13.29±7.40	17.90±7.09	13.14±7.02	16.79±8.60	14.19±6.07	13.47±6.87	11.28±4.64	12.11±6.27
Placebo, mean□SD	11.02±3.51	10.95±4.10	10.47±4.36	11.14±5.15	10.64±4.16	10.51±3.79	10.97±4.59	12.22±5.68	11.10±4.69	11.16±4.69
P value	0.516	<0.001	0.300	<0.001	0.222	0.003	0.062	0.357	0.779	0.810
CD8+ T cells (%)										
IL-2, mean□SD	46.17±12.37	41.94±12.16	46.68±13.23	46.32±12.00	48.76±13.62	47.54±13.06	46.42±13.68	45.21±12.62	47.93±13.69	46.19±12.06
Placebo, mean□SD	45.78±13.83	43.77±14.40	45.98±15.55	46.75±17.44	47.80±15.65	46.07±14.85	45.16±13.20	46.29±14.40	49.40±11.33	49.62±14.18
P value	0.774	0.550	0.856	0.824	0.912	0.742	0.740	0.712	0.795	0.438
NK cells (%)										
IL-2, mean□SD	6.48±4.85	10.40±7.13	7.99±5.68	10.51±6.09	9.44±4.52	12.07±8.01	10.20±8.05	9.13±5.83	8.93±6.24	7.28±4.15
Placebo, mean□SD	6.49±6.02	5.66±4.98	6.22±6.63	6.38±6.79	5.98±6.22	6.80±6.42	5.44±4.47	6.32±6.43	6.35±5.30	6.30±5.31
P value	0.786	0.001	0.101	0.001	0.001	0.005	0.001	0.012	0.053	0.210
CD56bri in NK cells (%)										
IL-2, mean□SD	6.68±4.45	13.19±8.82	7.58±5.53	10.89±6.93	6.40±4.46	10.40±6.49	6.54±4.07	6.03±4.40	5.55±4.25	6.70±5.46
Placebo, mean□SD	8.10±6.99	9.15±8.86	7.89±7.70	6.18±5.66	7.70±6.81	6.56±4.65	7.43±5.67	7.90±6.74	7.98±6.07	9.41±7.53
P value	0.635	0.030	0.743	0.004	0.737	0.022	0.712	0.376	0.078	0.140