

Supplementary Table S1. Baseline clinical characteristics and remission induction therapy between the patients whose CMV pp65 were antigen measured or not.

	CMV pp65 antigen measured (n=179)	CMV pp65 antigen not measured (n=96)	p-value
Age (years)*	57.1 ± 17.0	53.9 ± 17.1	0.15
Female, n (%)	123 (68.7%)	71 (74.0%)	0.36
Body weight (kg)*	53.9 ± 10.3	51.7 ± 10.0	0.10
Diagnosis			
SLE, n (%)	54 (30.2%)	32 (33.3%)	0.59
Vacuitides, n (%)	48 (26.8%)	16 (16.7%)	0.05
PM/DM, n (%)	24 (13.4%)	11 (11.5%)	0.64
RA, n (%)	21 (11.7%)	9 (9.4%)	0.55
AOSD, n (%)	10 (5.6%)	5 (5.2%)	0.90
SSc, n (%)	6 (3.4%)	3 (3.1%)	1.00
SS, n (%)	6 (3.4%)	1 (1.0%)	0.43
Others, n (%)	9 (5.0%)	19 (19.8%)	<0.01
Remission induction therapy			
GC use, n (%)	179 (100%)	96 (100%)	1.00
Initial GC dose as PSL (mg/kg/day)*	0.94 ± 0.18	0.73 ± 0.18	<0.01
mPSL pulse therapy, n (%)	55 (30.7%)	9 (14.1%)	<0.01
Concomitant IS use	129 (72.1%)	50 (52.1%)	<0.01
IVCY, n (%)	82 (45.8%)	18 (18.8%)	<0.01
AZP, n (%)	14 (7.8%)	7 (7.3%)	0.88
CI, n (%)	28 (15.6%)	15 (15.6%)	1.00
MTX, n (%)	9 (5.0%)	7 (7.3%)	0.45
MMF, n (%)	7 (3.9%)	4 (4.2%)	1.00
IFX, n (%)	1 (0.6%)	0 (0.0%)	1.00
TCZ, n (%)	7 (3.9%)	1 (1.0%)	0.29
ABT, n (%)	1 (0.6%)	0 (0.0%)	1.00
RTX, n (%)	1 (0.6%)	0 (0.0%)	1.00
Two or more ISs use, n (%)	22 (12.3%)	4 (4.2%)	0.03

CMV: cytomegalovirus; SLE: systemic lupus erythematosus; PM: polymyositis; DM: dermatomyositis; RA: rheumatoid arthritis; AOSD: adult-onset Still's disease; SSc: systemic sclerosis; SS: Sjögren's syndrome; GC: glucocorticoid; PSL: prednisolone; mPSL: methylprednisolone; IS: immunosuppressant; IVCY: intravenous cyclophosphamide; AZP: azathioprine; CI: calcineurin inhibitor; MTX: methotrexate; MMF: mycophenolate mofetil; IFX: infliximab; TCZ: tocilizumab; ABT: abatacept; RTX: rituximab. * mean ± SD.

Supplementary Table S2. Details of CMV disease.

CMV disease	n=19
Bone marrow suppression, n (%)	16 (84.2%)
Thrombocytopenia, n (%)	10 (52.6%)
Leukocytopenia, n (%)	1 (5.3%)
Thrombocytopenia + anaemia, n (%)	2 (10.5%)
Pancytopenia, n (%)	3 (15.8%)
Liver dysfunction, n (%)	2 (10.5%)
Retinitis, n (%)	1 (5.3%)
Pericarditis, n (%)	2 (10.5%)

CMV: cytomegalovirus.

Supplementary Table S3. Comparison of baseline characteristics, remission induction therapy, CMV reactivation, and anti-CMV treatment between asymptomatic CMV infection group with or without anti-CMV agent and CMV disease group.

	Asymptomatic CMV infection group cured without anti-CMV agent (n=26)	Asymptomatic CMV infection group with pre- emptive anti-CMV agent (n=26)	CMV disease group (n=19)	p-value
Age (years)*	57.7 ± 18.5	61.0 ± 14.2	64.4 ± 10.6	0.35
Female, n (%)	17 (65.4%)	15 (57.7%)	14 (73.7%)	0.54
Body weight (kg)*	53.6 ± 10.1	55.0 ± 11.8	53.3 ± 9.9	0.83
Diagnosis				
SLE, n (%)	9 (34.6%)	6 (23.1%)	7 (36.8%)	0.54
Vacuulitides, n (%)	10 (38.5%)	8 (30.8%)	2 (10.5%)	0.11
PM/DM, n (%)	0 (0.0%)	5 (19.2%)	2 (10.5%)	0.07
RA, n (%)	1 (3.8%)	5 (19.2%)	2 (10.5%)	0.21
AOSD, n (%)	1 (3.8%)	1 (3.8%)	3 (15.8%)	0.22
SSc, n (%)	2 (7.7%)	0 (0.0%)	0 (0.0%)	0.17
SS, n (%)	1 (3.8%)	1 (3.8%)	2 (10.5%)	0.56
Others, n (%)	2 (7.7%)	0 (0.0%)	1 (5.3%)	0.37
New-onset rheumatic disease, n (%)	16 (61.5%)	21 (80.8%)	14 (73.7%)	0.30
Disease duration (years)*	3.6 ± 5.8	4.3 ± 9.6	7.2 ± 13.7	0.46
Baseline laboratory findings				
White blood cell count (/μl)*	7985 ± 5275	9504 ± 6010	6462 ± 4351	0.17
Lymphocyte count (/μl)*	891 ± 585	973 ± 690	798 ± 523	0.64
Serum total protein (g/dl)*	6.3 ± 0.9	6.1 ± 0.9	6.5 ± 1.4	0.56
Serum albumin (g/dl)*	2.8 ± 0.6	2.6 ± 0.8	2.8 ± 0.6	0.41
Serum IgG (mg/dl)*	1703 ± 692	1469 ± 550	1908 ± 1044	0.17
Serum creatinine (mg/dl)*	1.20 ± 1.01	1.16 ± 1.22	1.00 ± 1.11	0.83
Serum CRP (mg/dl)*	5.29 ± 9.02	7.51 ± 7.67	4.19 ± 6.79	0.36
Remission induction therapy				
GC use, n (%)	26 (100%)	26 (100%)	26 (100%)	1.00
Initial GC dose as PSL (mg/kg/day)*	0.98 ± 0.18	0.99 ± 0.15	0.98 ± 0.16	0.98
mPSL pulse therapy, n (%)	15 (57.7%)	9 (34.6%)	8 (42.1%)	0.24
Concomitant IS use	19 (73.1%)	18 (69.2%)	15 (78.9%)	0.77
IVCY, n (%)	12 (46.2%)	17 (65.4%)	8 (42.1%)	0.23
AZP, n (%)	2 (7.7%)	0 (0.0%)	1 (5.3%)	0.37
CI, n (%)	1 (3.8%)	5 (19.2%)	1 (5.3%)	0.13
MTX, n (%)	1 (3.8%)	0 (0.0%)	1 (5.3%)	0.53
MMF, n (%)	3 (11.5%)	0 (0.0%)	0 (0.0%)	0.07
TCZ, n (%)	1 (3.8%)	1 (3.8%)	3 (15.8%)	0.22
ABT, n (%)	0 (0.0%)	0 (0.0%)	1 (5.3%)	0.25
Two or more ISs use, n (%)	1 (3.8%)	5 (19.2%)	0 (0.0%)	0.04
Period from start of induction therapy to CMV reactivation (days)*	26.7 ± 13.2	23.4 ± 14.9	19.3 ± 10.2	0.18
CMV pp65 antigen positive polymorphonuclear leukocytes at first reactivation (cells/2 slides)*	1.7 ± 1.3	6.1 ± 9.1	3.8 ± 6.5	0.05
Maximum CMV pp65 antigen polymorphonuclear leukocytes (cells/2 slides)*	2.0 ± 1.4	8.2 ± 11.1	21.5 ± 38.1	0.01
GC dose as PSL at first reactivation (mg/kg/day)*	0.76 ± 0.24	0.85 ± 0.19	0.88 ± 0.20	0.17
Anti-CMV agents, n (%)	–	26 (100%)	18 (94.7%)	0.42
GCV, n (%)	–	21 (80.8%)	14 (73.7%)	0.57
VGCV, n (%)	–	4 (15.4%)	4 (21.1%)	1.00
VGCV → Foscarnet, n (%)	–	1 (3.8%)	0 (0.0%)	1.00
Adverse events by anti-CMV agents, n (%)	–	1 (3.8%)	4 (21.1%)	0.15
Pancytopenia, n (%)	–	0 (0.0%)	1 (5.3%)	0.42
Leukocytopenia, n (%)	–	1 (3.8%)	2 (10.5%)	0.57
Serum CK elevation, n (%)	–	0 (0.0%)	1 (5.3%)	0.42
Period from CMV reactivation to CMV pp65 antigen disappearance (days)*	18.1 ± 12.4 (N=19)	18.3 ± 12.9 (N=24)	23.0 ± 12.4 (N=18)	0.40
GC dose as PSL at CMV pp65 antigen disappearance (mg/kg/day)*	0.59 ± 0.16	0.56 ± 0.16	0.56 ± 0.19	0.82
Observation period (weeks)*	79.1 ± 73.1	51.3 ± 43.7	70.2 ± 66.6	0.27

CMV: cytomegalovirus; SLE: systemic lupus erythematosus; PM: polymyositis; DM: dermatomyositis; RA: rheumatoid arthritis; AOSD: adult-onset Still's disease; SSc: systemic sclerosis; SS: Sjögren's syndrome; IgG: immunoglobulin G; CRP: C-reactive protein; GC: glucocorticoid; PSL: prednisolone; mPSL: methylprednisolone; IS: immunosuppressant; IVCY: intravenous cyclophosphamide; AZP: azathioprine; CI: calcineurin inhibitor; MTX: methotrexate; MMF: mycophenolate mofetil; TCZ: tocilizumab; ABT: abatacept; GCV: ganciclovir; VGCV: valganciclovir; CK: creatine kinase. * mean±SD.

Supplementary Table S4. Other infectious adverse events.

Infectious adverse events	CMV-positive group (n=71)		CMV-negative group (n=108)	
	no. of events	Events/100 person-years	no. of events	Events/100 person-years
Any other infectious event	111	122.5	66	40.3
Pathogen				
Bacterial	45	49.7	18	11.0
Viral	16	17.7	27	16.5
Fungal	49	43.1	21	12.8
Parasitic	1	1.1	0	0.0
Infected site				
Central nervous system	3	3.3	0	0.0
Mouth and upper respiratory tract	42	46.4	27	16.5
Lungs	30	33.1	12	7.3
Abdomen	13	14.4	3	1.8
Urinary tract	2	2.2	4	2.4
Skin	11	12.1	20	12.2
Severe infection	48	53.0	15	9.2
Bacterial pneumonia	22	24.3	10	6.1
Pneumocystis pneumonia	1	1.1	1	0.6
Nocardia lung abscess	1	1.1	0	0.0
Nocardia brain abscess	2	2.2	0	0.0
Aspergillosis	2	2.2	0	0.0
Nontuberculous mycobacteriosis	1	1.1	0	0.0
Clostridium difficile enteritis	2	2.2	0	0.0
Cholangitis	2	2.2	0	0.0
Appendicitis	1	1.1	0	0.0
Acute gastroenteritis	0	0.0	1	0.6
Intestinal necrosis	1	1.1	0	0.0
Panperitonitis	1	1.1	0	0.0
Campylobacter enteritis	0	0.0	1	0.6
Pyelonephritis	0	0.0	1	0.6
Herpes zoster encephalitis	1	1.1	0	0.0
Herpes zoster	3	3.3	0	0.0
Norway scabies	1	1.1	0	0.0
Cellulitis	0	0.0	1	0.6
Bacteraemia	9	9.9	0	0.0
Fungaemia	1	1.1	0	0.0

CMV: cytomegalovirus.

Supplementary Table S5. Causes of the death in each group.

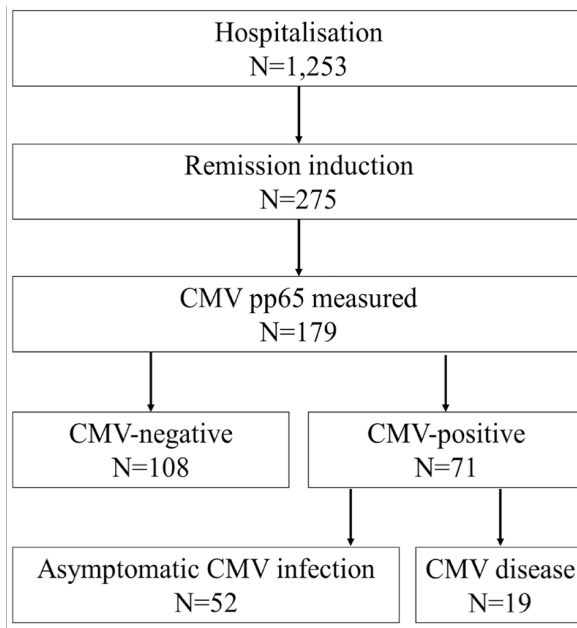
CMV-positive group	CMV-negative group
Sepsis (n=4)	Acute heart failure due to pulmonary arterial hypertension (n=1)
Severe pneumonia (n=3)	Sudden death (n=1)
Pneumocystis pneumonia (n=1)	
Exacerbation of interstitial lung disease (n=1)	
Rupture of aortic aneurysm (n=1)	

CMV: cytomegalovirus.

Supplementary Table S6. Lymphocyte counts and serum IgG levels.

	CMV reactivation			CMV disease		
	(-) n=108	(+) n=71	<i>p</i> -value	(-) n=160	(+) n=19	<i>p</i> -value
Lymphocyte count						
Mean (/μl)*	1580 ± 868	1103 ± 809	<0.01	1398 ± 849	985 ± 911	0.08
Minimum (/μl)*	989 ± 690	641 ± 550	<0.01	814 ± 653	558 ± 586	0.10
Serum IgG						
Mean (mg/dl)*	1149 ± 452	1263 ± 530	0.25	1112 ± 446	1055 ± 441	0.65
Minimum (mg/dl)*	1047 ± 429	1126 ± 443	0.36	956 ± 415	978 ± 430	0.86

CMV: cytomegalovirus; IgG: immunoglobulin G. * mean±SD.



Supplementary Fig. S1. Patient flow.

Among a total of 1,253 in-patients, 269 patients with rheumatic diseases received remission induction therapy. One hundred and seventy-nine patients out of them were measured CMV pp65 antigen and enrolled in the analysis. CMV was reactivated in 71 patients, and 19 patients developed CMV disease. CMV: cytomegalovirus.