**Supplementary text.** ICD-10 codes for detection of treatment episodes in patients with rheumatic diseases

Systemic lupus erythematosus (SLE, M32),

Systemic sclerosis (M34)

Dermatomyositis (M33.0, M33.1 and M33.9)

Polymyositis (M33.2)

Granulomatosis with polyangiitis (GPA, M31.3)

Microscopic polyangiitis (MPA, M31.7)

Eosinophilic granulomatosis with polyangiitis (EGPA, M30.1)

Polyarteritis nodosa (M30.0 and M30.8)

Rheumatoid arthritis (M05)

Adult-onset Still’s disease (AOSD, M06.1)

Behcet’s disease (M35.2)

Cryoglobulinemic vasculitis (D89.1)

Ankylosing spondylitis (M45)

Temporal arteritis (M31.5 and M31.6)

Polymyalgia rheumatica (M35.3)

Takayasu’s arteritis (M31.4)

Relapsing polychondritis (M94.1)

Sjogren syndrome (M35.0).

**Supplementary figure S1.** Algorithm for detecting PCP cases



**Supplementary figure S2.** Standardized difference of covariates before and after the propensity-score matching



**Supplementary table S1.** Summary of 30 PCP cases

|  |  |
| --- | --- |
| Age, mean (SD) | 46.9 (18.5) |
| Male gender, n (%) | 9 (30.0%) |
| SLE, n (%) | 15 (50.0%) |
| Systemic sclerosis, n (%) | 3 (10.0%) |
| GPA, n (%) | 2 (6.7%) |
| MPA, n (%) | 3 (10.0%) |
| Dermatomyositis, n (%) | 3 (10.0%) |
| Rheumatoid arthritis, n (%) | 1 (3.3%) |
| Cryoglobulinemic vasculitis, n (%) | 1 (3.3%) |
| Sjogren syndrome, n (%) | 1 (3.3%) |
| Temporal arteritis, n (%) | 1 (3.3%) |
| Cumulative steroid dose, mg, mean (SD)\* | 1477.8 (1198.5) |
| Duration of high-dose steroid treatment, days, mean (SD) | 77.1 (73.4) |
| Concomitant cyclophosphamide PO, n (%) | 2 (6.7) |
| Concomitant cyclophosphamide pulse, n (%) | 7 (23.3) |
| Concomitant steroid pulse, n (%) | 8 (26.7) |
| Baseline lymphopenia, n (%) | 13 (43.3) |
| Initial steroid dose, mg/day, mean(SD) | 76.0 (41.1) |
| Steroid dose at PCP, mg/day, median (minimum, maximum) \* | 27.5 (5.0, 80.0)) |
|  PCP occurred at 5~15mg/day of prednisone, n (%) | 3 (10.0) |
| PCP occurred at 15~30mg/day of prednisone, n (%) | 12 (40.0) |
| PCP occurred at 30mg/day or more of prednisone, n (%) | 15 (50.0) |
| Interval between the baseline and PCP, months, mean (SD) | 3.4 (2.5) |
| Bactrim prophylaxis, n (%) | 1 (3.3%) |

There were no PCP cases in other rheumatic diseases during the observation.

\*, indicates cumulatively used steroid (prednisone) dose during previous 6 months.

**Supplementary table S2.** Clinical features of the 30 PCP cases at diagnosis

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Case | Gender | Age | Underlying disease | Interval between baseline and PCP (month) | Lymphocyte count at baseline\* | Lymphocyte count at PCP\* | Steroid dose at PCP† (mg) | Period of maintaining steroid dose at PCP (day) | Concomitant cyclophosphamide pulse at baseline | PCP prophylaxis | PCP-related death |
| 1 | F | 49 | SLE | 3.1 | 770 | 157 | 50 | 93 | No | No | Yes |
| 2 | F | 37 | SLE | 3.4 | 1001 | 481 | 20 | 55 | Yes | No | No |
| 3 | F | 68 | GPA | 2.8 | 361 | 293 | 15 | 83 | No | No | Yes |
| 4 | F | 56 | SLE | 1.3 | 651 | 472 | 30 | 26 | No | No | Yes |
| 5 | M | 39 | SLE | 8.8 | 1379 | 634 | 10 | 54 | Yes | No | No |
| y | F | 53 | RA | 3.7 | 570 | 300 | 10 | 69 | No | Yes | No |
| 7 | M | 93 | MPA | 2.4 | 846 | 226 | 17.5 | 21 | No | No | Yes |
| 8 | F | 62 | Systemic sclerosis | 2.1 | 1303 | 271 | 30 | 54 | Yes | No | No |
| 9 | M | 47 | SLE | 5.3 | 2464 | 474 | 80 | 43 | No | No | Yes |
| 10 | M | 31 | Dermatomyositis | 10.8 | 4029 | 780 | 15 | 253 | Yes | No | No |
| 11 | F | 60 | SLE | 3.1 | 278 | 131 | 25 | 23 | No | No | Yes |
| 12 | F | 27 | SLE | 1.1 | 427 | 599 | 60 | 12 | Yes | No | No |
| 13 | F | 31 | SLE | 3.6 | 832 | 421 | 15 | 15 | No | No | No |
| 14 | F | 52 | Systemic sclerosis | 3.5 | 1829 | 192 | 15 | 1 | No | No | No |
| 15 | F | 22 | SLE | 3.9 | 338 | 348 | 15 | 8 | No | No | No |
| 16 | M | 56 | Systemic sclerosis | 1.4 | 2550 | 920 | 60 | 38 | No | No | Yes |
| 17 | M | 24 | Temporal arteritis | 3.5 | 966 | 722 | 30 | 26 | No | No | No |
| 18 | F | 75 | GPA | 2.2 | 1437 | 281 | 30 | 51 | No | No | Yes |
| 19 | F | 63 | MPA | 10.5 | 1488 | 307 | 5 | 116 | No | No | No |
| 20 | F | 23 | SLE | 1.5 | 129 | 167 | 60 | 16 | Yes | No | No |
| 21 | M | 39 | Dermatomyositis | 0.9 | 549 | 900 | 60 | 12 | No | No | Yes |
| 22 | F | 61 | Dermatomyositis | 2.8 | 771 | 407 | 15 | 20 | No | No | No |
| 23 | F | 18 | SLE | 3.9 | 1373 | 852 | 30 | 13 | No | No | No |
| 24 | F | 37 | SLE | 2.6 | 136 | 145 | 20 | 22 | No | No | No |
| 25 | M | 51 | Cryoglobulinemic vasculitis | 3.2 | 1151 | 1291 | 60 | 96 | No | No | No |
| 26 | F | 79 | MPA | 1.8 | 2725 | 620 | 20 | 37 | No | No | Yes |
| 27 | F | 45 | SLE | 1.4 | 285 | 510 | 30 | 29 | No | No | No |
| 28 | F | 33 | SLE | 1.7 | 980 | 320 | 60 | 25 | Yes | No | Yes |
| 29 | M | 24 | SLE | 2.6 | 1091 | 314 | 25 | 38 | No | No | No |
| 30 | F | 52 | Sjogren syndrome | 3.9 | 560 | 787 | 40 | 39 | No | No | No |

\*, indicates the lymphocyte counts per milliliter

†, based on the dose of prednisone, mg/day

**Supplementary table S3** Clinical factors which influence on 1-year PCP incidence and its related mortality in the propensity score-matched population

|  |  |  |  |
| --- | --- | --- | --- |
|  | 1-year PCP incidence |  | 1-year PCP-related mortality |
|  | Hazard ratio (95% CI) |  | Hazard ratio (95% profile likelihood CI) |
| Clinical factors | Univariable analysis | Multivariable analysis\* |  | Univariable analysis | Multivariable analysis\* |
| Age | 1.03 (0.997-1.06) | 1.02 (0.98-1.06) |  | 1.08 (1.03-1.15) | 1.05 (0.99-1.12) |
| Male gender | 0.89 (0.28-2.79) | ‡ |  | 0.90 (0.22-5.00) | ‡ |
| SLE | 0.74 (0.27-2.09) | ‡ |  | 0.86 (0.19-3.54) | ‡ |
| Dermatomyositis | 0.41 (0.05-3.14) | ‡ |  | 0.39 (0.003-3.18) | ‡ |
| GPA | 2.37 (0.54-10.51) | ‡ |  | 6.95 (1.25-28.81) | 5.74 (0.90-32.48) |
| MPA | 5.11 (1.15-22.64) | 3.52 (0.71-17.52) |  | 14.91 (2.68-61.85) | 8.27 (0.84-93.52) |
| Higher initial steroid dose (≥60mg PD) | 2.24 (0.71-7.02) | ‡ |  | 1.78 (0.43-9.89) | ‡ |
| Concomitant cyclophosphamide pulse | 1.28 (0.41-4.03) | ‡ |  | 0.80 (0.08-3.82) | ‡ |
| Concomitant oral cyclophosphamide | 1.45 (0.33-6.42) | ‡ |  | 2.22 (0.23-10.55) | ‡ |
| Concomitant steroid pulse | 1.27 (0.45-3.56) | ‡ |  | 1.47 (0.33-6.02) | ‡ |
| Baseline lymphopenia † | 1.11 (0.38-3.23) | ‡ |  | 1.00 (0.18-4.15) | ‡ |
| TMP-SMX prophylaxis  | 0.07 (0.01-0.54) | 0.07 (0.01-0.53) |  | 0.07 (0.0005-0.55) | 0.08 (0.0006-0.71) |

CI, confidence interval; PD, prednisone; TMP-SMX, trimethoprim-sulfamethoxazole.

\* Model included clinical factors which showed significant association (*p*<0.1) in the univariable analysis and was adjusted for clustering.

† Defined as less than 800 lymphocytes per microliter

‡ Not included in the multivariable model due to lack of significant association in the univariable analysis

**Supplementary table S4.** Clinical factors which influence on 1-year PCP incidence and its related mortality in the whole population

|  |  |  |  |
| --- | --- | --- | --- |
|  | 1-year PCP incidence |  | 1-year PCP-related mortality |
|  | Hazard ratio (95% CI) |  | Hazard ratio (95% profile likelihood CI) |
| Clinical factors | Univariable analysis | Multivariable analysis\* |  | Univariable analysis | Multivariable analysis\* |
| Age | 1.02 (0.998-1.04) | 1.02 (1.00-1.05) |  | 1.08 (1.03-1.12) | 1.06 (1.01-1.11) |
| Male gender | 0.98 (0.45-2.15) | ‡ |  | 0.72 (0.23-2.56) | ‡ |
| SLE | 1.00 (0.49-2.05) | ‡ |  | 0.84 (0.26-2.66) | ‡ |
| Dermatomyositis | 1.12 (0.34-3.68) | ‡ |  | 1.43 (0.15-6.10) | ‡ |
| GPA | 1.91 (0.45-8.01) | ‡ |  | 7.00 (1.34-24.70) | 4.79 (0.86-19.34) |
| MPA | 9.42 (2.86-31.06) | 14.70 (3.21-67.30) |  | 21.99 (4.20-77.55) | 7.58 (0.92-59.40) |
| Higher initial steroid dose (≥60mg PD) | 2.35 (1.05-5.27) | 2.37 (1.03-5.48) |  | 2.06 (0.64-8.36) | ‡ |
| Concomitant cyclophosphamide pulse | 2.55 (1.09-5.94) | 2.82 (1.04-7.67) |  | 2.17 (0.42-7.65) | ‡ |
| Concomitant oral cyclophosphamide | 1.26 (0.30-5.27) | ‡ |  | 2.52 (0.27-10.70) | ‡ |
| Concomitant steroid pulse | 1.68 (0.79-3.97) | ‡ |  | 2.90 (0.82-9.13) | 2.89 (0.67-10.35) |
| Baseline lymphopenia † | 2.44 (1.18-5.02) | 2.58 (1.22-5.46) |  | 2.66 (0.81-8.40) | ‡ |
| TMP-SMX prophylaxis  | 0.17 (0.02-1.22) | 0.06 (0.004-0.66) |  | 0.21 (0.002-1.61) | 0.09 (0.0007-0.76) |

CI, confidence interval; PD, prednisone; TMP-SMX, trimethoprim-sulfamethoxazole.

\* Model included clinical factors which showed significant association (*p*<0.1) in the univariable analysis and was adjusted for clustering.

† Defined as less than 800 lymphocytes per microliter

‡ Not included in the multivariable model due to lack of significant association in the univariable analysis

**Supplementary figure S3.** Kaplan-Meier curve indicating PCP occurrence between the two groups until the steroid dose was tapered by (A) 30mg/day of prednisone and (B) 15mg/day of prednisone. If a patient stopped TMP-SMX at higher-dose of steroid than above, observation was stopped at the last day of prophylaxis. Both sensitivity analyses, TMP-SMX significantly reduced the PCP occurrence.





**Supplementary figure S4.** Kaplan-Meier curve indicating PCP occurrence between two groups using observation period of (A) 6-month and (B) 3-month. This resulted in significant increase in the proportion of time that TMP-SMX was administered as compared with that in the original analysis (0.50 [0.33] in 1-year, 0.70[0.32] in 6-month and 0.86 [0.25] in 3-month p<0.001 using one-way ANOVA). However, the efficacy of prophylactic TMP-SMX was not changed.



