

## **SUPPLEMENTARY MATERIALS**

### **Association Between Mycophenolate Mofetil Use and Subsequent Infections Among Hospitalized Patients with Systemic Lupus Erythematosus: A Nested Case–Control Study**

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**Supplementary Table 1. Infection classifications by key words in hospital discharge diagnosis.**

| Types of infections      | Infection name                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|--------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Bacterial infections     | Bacterial<br>Pneumonia<br>Sepsis-/Septic-<br>Bacteremia<br>Staphylococcus aureus sepsis<br>Enterobacteriaceae infectious bacteraemia<br>Staphylococcus epidermidis septicaemia<br>Staphylococcus faecalis septicaemia<br>Pyogenic<br>Abscess<br>Suppurative inflammation<br>Pyelonephritis<br>Salmonella typhimurium enteritis<br>Salmonella infection<br>Helicobacter pylori infection<br>Haemophilus influenzae infection<br>Pyelonephritis<br>Bacterial vaginosis<br>Group B streptococcal infection<br>Streptococcus vaginalis infection<br>Cellulitis/Cellulitic |
| Virus infections         | Viral<br>Herpes zoster/HZV<br>Epstein-Barr virus/EBV<br>Herpes virus<br>Cytomegalovirus/CMV<br>Viral hepatitis<br>Human papilloma virus/HPV<br>Syphilis<br>Viral encephalitis<br>Viral meningitis<br>Viral myocarditis<br>Minute virus B19 infection<br>Cytomegalovirus haemorrhage<br>Viral warts<br>Viral upper respiratory tract infection<br>Viral conjunctivitis<br>Influenza virus                                                                                                                                                                              |
| Opportunistic infections | Tuberculous<br>Tuberculosis<br>Mycobacterial infection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

|                                   |                                                                                                                                                                                                                                                                                                                                                                                  |
|-----------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                   | Mycosis<br>Fungal<br>Candida infection<br>Aspergillus infection<br>Cryptococcal infection<br>Aspergillus infection<br>Malassezia folliculitis<br>Pneumocystis carinii pneumonia<br>Cutaneous Nocardia<br>Cryptococcosis<br>Aspergillosis<br>Histoplasmosis<br>Pneumocystosis                                                                                                     |
| Other infections of unknown cause | Upper respiratory tract infections<br>Urinary tract infections<br>Pancreatitis<br>Gastrointestinal tract infections<br>Soft tissue skin infections<br>Infectious fever<br>Abdominal infection<br>Thoracic infection<br>Infectious shock<br>Infective endocarditis<br>Myocarditis<br>Skin ulcers with infection<br>Bone and joint infections<br>Central nervous system infections |

**Supplementary Table 2. Characteristics of Systemic lupus erythematosus (SLE) patients by status of infection after Propensity score matching (PSM).**

| Variables                                | Infection patients    | No infection patients | <i>P</i> <sup>b</sup> |
|------------------------------------------|-----------------------|-----------------------|-----------------------|
| Total                                    | n = 1449              | n = 1449              |                       |
| Gender (female), n (%)                   | 1291 (89.1)           | 1305 (90.1)           | 0.395                 |
| Age (years), median (IQR)                | 37.0 (27.0, 50.0)     | 36.0 (27.0, 48.0)     | 0.456                 |
| SLE disease period (years), median (IQR) | 3.0 (0, 10.0)         | 3.0 (0, 10.0)         | 0.181                 |
| SLEDAI score on admission, median (IQR)  | 12.0 (6.0,17.0)       | 11.0 (6.0,17.0)       | 0.197                 |
| BMI, median (IQR)                        | 21.3 (19.3, 24.2)     | 22.1 (19.8, 24.5)     | <b>0.004</b>          |
| Smoking, n (%)                           | 70 (4.8)              | 64 (4.4)              | 0.596                 |
| Drinking, n (%)                          | 51 (3.5)              | 46 (3.2)              | 0.606                 |
| Hypertension, n (%)                      | 513 (35.4)            | 444 (30.6)            | <b>0.006</b>          |
| Diabetes mellitus, n (%)                 | 135 (9.3)             | 78 (5.4)              | <b>&lt; 0.001</b>     |
| Clinical manifestations of SLE, n (%)    |                       |                       |                       |
| Rash                                     | 413 (28.5)            | 463 (32.0)            | <b>0.043</b>          |
| Vasculitis                               | 133 (9.2)             | 157 (10.8)            | 0.137                 |
| Arthritis                                | 232 (16.0)            | 269 (18.6)            | 0.069                 |
| Serositis                                | 693 (47.8)            | 494 (34.1)            | <b>&lt; 0.001</b>     |
| Renal involvement                        | 788 (54.4)            | 735 (50.7)            | <b>0.049</b>          |
| CNS involvement                          | 137 (9.5)             | 125 (8.6)             | 0.437                 |
| Hematological involvement                | 1220 (84.2)           | 1080 (74.5)           | <b>&lt; 0.001</b>     |
| Laboratory features, median (IQR)        |                       |                       |                       |
| ESR (mm/h)                               | 44.0 (23.0, 73.0)     | 33.5 (17.0, 58.0)     | <b>&lt; 0.001</b>     |
| C-reactive protein                       | 6.8 (3.2, 30.0)       | 3.7 (2.1, 6.7)        | <b>&lt; 0.001</b>     |
| A/G, median (IQR)                        | 1.3 (1.0, 1.5)        | 1.3 (1.1, 1.6)        | <b>0.015</b>          |
| ALB (g/L)                                | 33.0 (28.5, 36.4)     | 34.1 (29.8, 37.9)     | <b>&lt; 0.001</b>     |
| GLB (g/L)                                | 25.8 (21.2, 31.0)     | 26.1 (21.4, 30.7)     | 0.296                 |
| WBC (10 <sup>9</sup> /L)                 | 5.4 (3.5, 8.1)        | 5.3 (3.6, 7.5)        | 0.139                 |
| NE (10 <sup>9</sup> /L)                  | 3.9 (2.4, 6.3)        | 3.7 (2.3, 5.6)        | <b>&lt; 0.001</b>     |
| LYM (10 <sup>9</sup> /L)                 | 0.9 (0.5, 1.3)        | 1.1 (0.7, 1.6)        | <b>&lt; 0.001</b>     |
| PLT (10 <sup>9</sup> /L)                 | 156.0 (98.0, 219.0)   | 166.0 (111.0, 219.0)  | <b>0.007</b>          |
| Hb (g/L)                                 | 102.0 (84.0, 118.0)   | 109.0 (93.0, 124.0)   | <b>&lt; 0.001</b>     |
| 24h urine protein (mg/d)                 | 747.0 (265.0, 2419.0) | 831.0 (221.0, 2517.5) | 0.762                 |
| eGFR-MDRD (mL/min·1.73 m <sup>2</sup> )  | 114.1 (72.7, 151.6)   | 123.4 (89.6, 159.4)   | <b>&lt; 0.001</b>     |
| Creatinine (μmol/L)                      | 56.0 (44.0, 85.0)     | 53.0 (43.0, 72.0)     | <b>&lt; 0.001</b>     |
| Anti-dsDNA antibody positive, n (%)      | 204 (14.1)            | 232 (16.0)            | 0.146                 |
| Hypocomplement, n (%)                    | 865 (59.7)            | 912 (62.9)            | 0.073                 |
| C3 (g/L), median (IQR)                   | 0.8 (0.5, 1.0)        | 0.7 (0.5, 1.0)        | 0.146                 |
| C4 (g/L), median (IQR)                   | 0.2 (0.1, 0.2)        | 0.1 (0.1, 0.2)        | <b>&lt; 0.001</b>     |
| Medications <sup>a</sup>                 |                       |                       |                       |
| Hydroxychloroquine, n (%)                | 1049 (72.4)           | 1035 (71.4)           | 0.563                 |

|                                                             |                   |                   |                   |
|-------------------------------------------------------------|-------------------|-------------------|-------------------|
| Glucocorticoids, n (%)                                      | 1365 (94.2)       | 1279 (88.3)       | <b>&lt; 0.001</b> |
| Mean daily prednisone- equivalent dose (mg/d), median (IQR) | 25.0 (10.0, 50.0) | 20.0 (10.0, 50.0) | <b>0.024</b>      |
| Cyclophosphamide, n (%)                                     | 363 (25.1)        | 156 (10.8)        | <b>&lt; 0.001</b> |
| Mycophenolate mofetil, n (%)                                | 235 (16.2)        | 91 (6.3)          | <b>&lt; 0.001</b> |
| Tacrolimus, n (%)                                           | 258 (17.8)        | 197 (13.6)        | <b>0.002</b>      |
| Leflunomide, n (%)                                          | 265 (18.3)        | 129 (8.9)         | <b>&lt; 0.001</b> |
| Methotrexate, n (%)                                         | 48 (3.3)          | 25 (1.7)          | <b>0.006</b>      |
| Cyclosporin A, n (%)                                        | 74 (5.1)          | 35 (2.4)          | <b>&lt; 0.001</b> |
| Azathioprine, n (%)                                         | 37 (2.6)          | 21 (1.4)          | <b>0.034</b>      |
| Thalidomide, n (%)                                          | 90 (6.2)          | 52 (3.6)          | <b>0.001</b>      |
| Tripterygium glycosides, n (%)                              | 126 (8.7)         | 40 (2.8)          | <b>&lt; 0.001</b> |

BMI: Body Mass Index; SLEDAI: systemic lupus erythematosus disease activity index; CNS: central nervous system; ESR: erythrocyte sedimentation rate; A/G: albumin/globulin ratio; ALB: albumin; GLB: globulin; WBC: white blood cells; NE: neutrophils; LYM: lymphocytes; PLT: platelets; Hb: hemoglobin; eGFR-MDRD: estimated glomerular filtration rate by modification of diet in renal disease. <sup>a</sup> Medications were the presence drugs within 365 days before diagnose infection or the end of follow-up. <sup>b</sup> Significant values are bolded.

**Supplementary Table 3. The associations between MMF use and risks of infections in SLE patients after PSM.**

| <b>Variable</b>                              | <b>MMF Users<br/>(N = 326)</b> | <b>Non-users<br/>(N = 2572)</b> | <b>OR<br/>(95% CI)</b>   | <b>Adjusted OR<br/>(95% CI)</b> |
|----------------------------------------------|--------------------------------|---------------------------------|--------------------------|---------------------------------|
| <b>No infection</b>                          | 91 (27.9)                      | 1358 (52.8)                     | 1.00                     | 1.00                            |
| <b>Overall infection</b>                     | 235 (72.1)                     | 1214 (47.2)                     | <b>2.89 (2.24, 3.72)</b> | <b>2.25 (1.72, 2.95)</b>        |
| Single infection                             | 191 (58.6)                     | 1024 (39.8)                     | <b>2.78 (2.14, 3.62)</b> | <b>2.19 (1.66, 2.90)</b>        |
| Complex infection                            | 44 (13.5)                      | 190 (7.4)                       | <b>3.46 (2.34, 5.11)</b> | <b>2.48 (1.61, 3.83)</b>        |
| <b>Bacterial infection</b>                   | 133 (40.8)                     | 684 (26.6)                      | <b>2.90 (2.19, 3.85)</b> | <b>2.26 (1.67, 3.06)</b>        |
| Urinary tract<br>infection/pyelonephritis    | 35 (10.7)                      | 123 (4.8)                       | <b>4.25 (2.76, 6.54)</b> | <b>3.05 (1.90, 4.90)</b>        |
| Pneumonia                                    | 86 (26.4)                      | 508 (19.8)                      | <b>2.53 (1.85, 3.45)</b> | <b>2.01 (1.44, 2.82)</b>        |
| Encephalitis/meningitis                      | 2 (0.6)                        | 17 (0.7)                        | 1.76 (0.40, 7.72)        | 1.44 (0.30, 6.91)               |
| Endocarditis/myocarditis                     | 2 (0.6)                        | 8 (0.3)                         | 3.73 (0.78, 17.82)       | 3.30 (0.61, 17.83)              |
| Septic<br>arthritis/osteomyelitis            | 0 (0)                          | 3 (0.1)                         | --                       | --                              |
| Septicemia/bacteremia                        | 7 (2.1)                        | 27 (1.0)                        | <b>3.87 (1.64, 9.12)</b> | <b>3.52 (1.37, 9.00)</b>        |
| <b>Virus infection</b>                       | 32 (9.8)                       | 195 (7.6)                       | <b>2.45 (1.59, 3.76)</b> | <b>1.99 (1.25, 3.16)</b>        |
| Herpes zoster                                | 10 (3.1)                       | 35 (1.4)                        | <b>4.26 (2.05, 8.88)</b> | <b>3.02 (1.35, 6.73)</b>        |
| HCMV infection                               | 2 (0.6)                        | 15 (0.6)                        | 1.99 (0.45, 8.83)        | 1.62 (0.32, 8.11)               |
| EBV infection                                | 11 (3.3)                       | 63 (2.4)                        | <b>2.61 (1.33, 5.12)</b> | <b>2.26 (1.08, 4.74)</b>        |
| HPV infection                                | 0 (0)                          | 4 (0.2)                         | --                       | --                              |
| Virus hepatitis                              | 4 (1.2)                        | 56 (2.2)                        | 1.07 (0.38, 3.01)        | 0.89 (0.30, 2.64)               |
| <b>Opportunistic infection</b>               | 31 (9.5)                       | 122 (4.7)                       | <b>3.79 (2.42, 5.93)</b> | <b>2.62 (1.60, 4.29)</b>        |
| Tuberculosis                                 | 9 (2.8)                        | 45 (1.7)                        | <b>2.99 (1.42, 6.30)</b> | <b>2.49 (1.11, 5.61)</b>        |
| Systemic mycoses                             | 22 (6.7)                       | 81 (3.1)                        | <b>4.05 (2.42, 6.80)</b> | <b>2.60 (1.47, 4.62)</b>        |
| <b>Other infections of<br/>unknown cause</b> | 59 (18.1)                      | 304 (11.8)                      | <b>2.90 (2.04, 4.11)</b> | <b>2.19 (1.50, 3.19)</b>        |
| Upper respiratory<br>infection               | 50 (15.3)                      | 285 (11.1)                      | <b>2.62 (1.81, 3.78)</b> | <b>1.79 (1.20, 2.67)</b>        |
| Skin or mucosal infection                    | 21 (6.4)                       | 83 (3.2)                        | <b>3.78 (2.24, 6.37)</b> | <b>2.86 (1.61, 5.09)</b>        |

HCMV; human cytomegalovirus, EBV: Epstein-Barr virus, HPV: human papilloma virus, MMF: mycophenolate mofetil, OR: odds ratio, CI: confidence interval. Multivariable analysis models were adjusted for hypertension (yes = 1, no = 0), diabetes mellitus (yes = 1, no = 0), mean daily prednisone equivalent dose (continuous), CYC treatment (yes = 1, no = 0), TAC treatment (yes = 1, no = 0), and other immunosuppressants (yes = 1, no = 0). Significant values are bolded.

**Supplementary Table 4. Major risk factors for overall infection in SLE patients.**

| <b>Variable</b>                       | <b>OR (95% CI)</b>       | <b>Adjusted OR (95% CI) <sup>d</sup></b> |
|---------------------------------------|--------------------------|------------------------------------------|
| Gender (female) <sup>a</sup>          | <b>1.31 (1.05, 1.64)</b> | <b>1.37 (1.08, 1.73)</b>                 |
| Age (years)                           | <b>1.01 (1.01, 1.02)</b> | <b>1.01 (1.01, 1.02)</b>                 |
| Course of disease (years)             | <b>1.01 (1.01, 1.02)</b> | <b>1.01 (1.00, 1.02)</b>                 |
| SLEDAI score                          | <b>1.04 (1.03, 1.05)</b> | <b>1.04 (1.03, 1.05)</b>                 |
| Hypertension <sup>b</sup>             | <b>1.44 (1.25, 1.67)</b> | 0.93 (0.79, 1.10)                        |
| Diabetes mellitus <sup>b</sup>        | <b>2.05 (1.57, 2.67)</b> | <b>1.71 (1.28, 2.28)</b>                 |
| CYC treatment <sup>b</sup>            | <b>2.71 (2.24, 3.28)</b> | <b>1.90 (1.53, 2.35)</b>                 |
| MMF treatment <sup>b</sup>            | <b>2.58 (2.05, 3.24)</b> | <b>1.90 (1.48, 2.44)</b>                 |
| TAC treatment <sup>b</sup>            | <b>1.42 (1.17, 1.71)</b> | 1.10 (0.89, 1.36)                        |
| HCQ treatment <sup>b</sup>            | 1.06 (0.91, 1.23)        | 1.03 (0.88, 1.22)                        |
| Other immunosuppressants <sup>b</sup> | <b>2.21 (1.87, 2.62)</b> | <b>1.59 (1.31, 1.93)</b>                 |
| Daily GCs > 20 mg/d <sup>c</sup>      | <b>1.19 (1.04, 1.36)</b> | <b>1.28 (1.10, 1.49)</b>                 |

SLEDAI: systemic lupus erythematosus disease activity index; CYC: cyclophosphamide; MMF: mycophenolate mofetil; TAC: tacrolimus; HCQ: hydroxychloroquine; GCs: glucocorticoid, all classes of GCs were converted to equivalent doses of prednisone; Other immunosuppressants: include leflunomide, methotrexate, cyclosporin A, azathioprine, thalidomide, and tripterygium glycosides; OR: odds ratio; CI: confidence interval. a: Male were used as the reference group; b: Non-use as the reference group; c: The reference group was GCs ≤ 20 mg/d; d: Multivariable analysis model is the mutual adjustment of variables in the table. Significant values are bolded.

**Supplementary Table 5. Joint effects of MMF and other major drugs on bacterial infection of SLE patients.**

| Variables                                   | MMF | Bacterial infection patients, n (%) (n = 912) | No infection patients, n (%) (n = 1762) | OR (95% CI)       | Adjusted OR (95% CI) |
|---------------------------------------------|-----|-----------------------------------------------|-----------------------------------------|-------------------|----------------------|
| <b>CYC</b>                                  |     |                                               |                                         |                   |                      |
| No                                          | No  | 625 (29.6)                                    | 1490 (70.4)                             | 1.00              | 1.00                 |
| No                                          | Yes | 67 (44.4)                                     | 84 (55.6)                               | 1.90 (1.36, 2.66) | 2.00 (1.39, 2.86)    |
| Yes                                         | No  | 140 (48.3)                                    | 150 (51.7)                              | 2.23 (1.74, 2.85) | 1.71 (1.29, 2.25)    |
| Yes                                         | Yes | 80 (67.8)                                     | 38 (32.2)                               | 5.02 (3.37, 7.47) | 3.74 (2.41, 5.78)    |
|                                             | ROR |                                               |                                         | 1.19 (0.68, 2.08) | 1.10 (0.61, 1.97)    |
| <b>TAC</b>                                  |     |                                               |                                         |                   |                      |
| No                                          | No  | 653 (31.1)                                    | 1449 (68.9)                             | 1.00              | 1.00                 |
| No                                          | Yes | 108 (56.0)                                    | 85 (44.0)                               | 2.82 (2.09, 3.80) | 2.28 (1.64, 3.18)    |
| Yes                                         | No  | 112 (37.0)                                    | 191 (63.0)                              | 1.30 (1.01, 1.67) | 1.14 (0.87, 1.50)    |
| Yes                                         | Yes | 39 (51.3)                                     | 37 (48.7)                               | 2.34 (1.48, 3.70) | 1.76 (1.05, 2.93)    |
|                                             | ROR |                                               |                                         | 0.64 (0.35, 1.15) | 0.67 (0.36, 1.26)    |
| <b>Daily GCs</b>                            |     |                                               |                                         |                   |                      |
| ≤ 20 mg                                     | No  | 312 (28.0)                                    | 804 (72.0)                              | 1.00              | 1.00                 |
| ≤ 20 mg                                     | Yes | 97 (53.6)                                     | 84 (46.4)                               | 2.98 (2.16, 4.10) | 2.49 (1.75, 3.53)    |
| > 20 mg                                     | No  | 453 (35.1)                                    | 836 (64.9)                              | 1.40 (1.17, 1.66) | 1.39 (1.15, 1.69)    |
| > 20 mg                                     | Yes | 50 (56.8)                                     | 38 (43.2)                               | 3.39 (2.18, 5.27) | 2.29 (1.41, 3.72)    |
|                                             | ROR |                                               |                                         | 0.82 (0.48, 1.40) | 0.66 (0.37, 1.18)    |
| <b>HCQ</b>                                  |     |                                               |                                         |                   |                      |
| Yes                                         | No  | 535 (31.6)                                    | 1157 (68.4)                             | 1.00              | 1.00                 |
| Yes                                         | Yes | 92 (50.8)                                     | 89 (49.2)                               | 2.24 (1.64, 3.05) | 1.80 (1.27, 2.53)    |
| No                                          | No  | 230 (32.3)                                    | 483 (67.7)                              | 1.03 (0.85, 1.24) | 1.06 (0.86, 1.30)    |
| No                                          | Yes | 55 (62.5)                                     | 33 (37.5)                               | 3.60 (2.31, 5.62) | 2.88 (1.78, 4.65)    |
|                                             | ROR |                                               |                                         | 1.57 (0.90, 2.72) | 1.52 (0.84, 2.74)    |
| <b>Other immunosuppressants<sup>a</sup></b> |     |                                               |                                         |                   |                      |
| No                                          | No  | 597 (29.8)                                    | 1408 (70.2)                             | 1.00              | 1.00                 |
| No                                          | Yes | 54 (42.2)                                     | 74 (57.8)                               | 1.72 (1.20, 2.48) | 1.75 (1.18, 2.58)    |
| Yes                                         | No  | 168 (42.0)                                    | 232 (58.0)                              | 1.71 (1.37, 2.13) | 1.47 (1.15, 1.89)    |
| Yes                                         | Yes | 93 (66.0)                                     | 48 (34.0)                               | 4.57 (3.18, 6.56) | 3.71 (2.48, 5.55)    |
|                                             | ROR |                                               |                                         | 1.56 (0.91, 2.67) | 1.44 (0.82, 2.55)    |

MMF: mycophenolate mofetil, CYC: cyclophosphamide, TAC: tacrolimus, GCs: glucocorticoids, all classes of GCs were converted to equivalent prednisone doses, HCQ: hydroxychloroquine, OR: odds ratio, CI: confidence interval, ROR is ratio of ORs. Multivariable analysis models were adjusted for gender (female = 1, male = 0), age (continuous), SLE disease period years (continuous), SLEDAI score on admission (continuous), hypertension (yes = 1, no = 0), diabetes mellitus (yes = 1, no = 0), mean daily prednisone equivalent dose (continuous), CYC treatment (yes = 1, no = 0), TAC treatment (yes = 1, no = 0), and other immunosuppressants (yes = 1, no = 0). <sup>a</sup> Other immunosuppressants included leflunomide, methotrexate, cyclosporin A, azathioprine, thalidomide and tripterygium glycosides.

**Supplementary Table 6. Joint effects of MMF and other major drugs on virus infection of SLE patients.**

| Variables                                   | MMF | Virus infection patients, n (%)<br>(n = 243) | No infection patients, n (%)<br>(n = 1762) | OR<br>(95% CI)    | Adjusted OR<br>(95% CI) |
|---------------------------------------------|-----|----------------------------------------------|--------------------------------------------|-------------------|-------------------------|
| <b>CYC</b>                                  |     |                                              |                                            |                   |                         |
| No                                          | No  | 168 (10.1)                                   | 1490 (89.9)                                | 1.00              | 1.00                    |
| No                                          | Yes | 17 (16.8)                                    | 84 (83.2)                                  | 1.80 (1.04, 3.10) | 1.92 (1.08, 3.43)       |
| Yes                                         | No  | 39 (20.6)                                    | 150 (79.4)                                 | 2.31 (1.57, 3.40) | 1.66 (1.07, 2.56)       |
| Yes                                         | Yes | 19 (33.3)                                    | 38 (66.7)                                  | 4.44 (2.50, 7.87) | 3.18 (1.67, 6.06)       |
|                                             | ROR |                                              |                                            | 1.07 (0.46, 2.51) | 1.00 (0.41, 2.42)       |
| <b>TAC</b>                                  |     |                                              |                                            |                   |                         |
| No                                          | No  | 177 (10.9)                                   | 1449 (89.1)                                | 1.00              | 1.00                    |
| No                                          | Yes | 24 (22.0)                                    | 85 (78.0)                                  | 2.31 (1.43, 3.73) | 1.98 (1.17, 3.36)       |
| Yes                                         | No  | 30 (13.6)                                    | 191 (86.4)                                 | 1.29 (0.85, 1.95) | 1.16 (0.74, 1.80)       |
| Yes                                         | Yes | 12 (24.5)                                    | 37 (75.5)                                  | 2.66 (1.36, 5.19) | 2.05 (0.99, 4.28)       |
|                                             | ROR |                                              |                                            | 0.89 (0.37, 2.19) | 0.90 (0.35, 2.30)       |
| <b>Daily GCs</b>                            |     |                                              |                                            |                   |                         |
| ≤ 20 mg                                     | No  | 94 (10.5)                                    | 804 (89.5)                                 | 1.00              | 1.00                    |
| ≤ 20 mg                                     | Yes | 19 (18.4)                                    | 84 (81.6)                                  | 1.94 (1.13, 3.33) | 1.86 (1.04, 3.31)       |
| > 20 mg                                     | No  | 113 (11.9)                                   | 836 (88.1)                                 | 1.16 (0.87, 1.55) | 1.23 (0.89, 1.68)       |
| > 20 mg                                     | Yes | 17 (30.9)                                    | 38 (69.1)                                  | 3.83 (2.08, 7.05) | 2.47 (1.24, 4.91)       |
|                                             | ROR |                                              |                                            | 1.71 (0.76, 3.85) | 1.09 (0.46, 2.58)       |
| <b>HCQ</b>                                  |     |                                              |                                            |                   |                         |
| Yes                                         | No  | 157 (11.9)                                   | 1157 (88.1)                                | 1.00              | 1.00                    |
| Yes                                         | Yes | 25 (21.9)                                    | 89 (78.1)                                  | 2.07 (1.29, 3.33) | 1.87 (1.11, 3.15)       |
| No                                          | No  | 50 (9.4)                                     | 483 (90.6)                                 | 0.76 (0.55, 1.07) | 0.75 (0.52, 1.07)       |
| No                                          | Yes | 11 (25.0)                                    | 33 (75.0)                                  | 2.46 (1.22, 4.96) | 1.67 (0.78, 3.59)       |
|                                             | ROR |                                              |                                            | 1.56 (0.65, 3.75) | 1.20 (0.47, 3.07)       |
| <b>Other immunosuppressants<sup>a</sup></b> |     |                                              |                                            |                   |                         |
| No                                          | No  | 155 (9.9)                                    | 1408 (90.1)                                | 1.00              | 1.00                    |
| No                                          | Yes | 12 (14.0)                                    | 74 (86.0)                                  | 1.47 (0.78, 2.77) | 1.63 (0.84, 3.15)       |
| Yes                                         | No  | 52 (18.3)                                    | 232 (81.7)                                 | 2.04 (1.44, 2.87) | 1.75 (1.19, 2.58)       |
| Yes                                         | Yes | 24 (33.3)                                    | 48 (66.7)                                  | 4.54 (2.71, 7.62) | 3.90 (2.14, 7.08)       |
|                                             | ROR |                                              |                                            | 1.51 (0.64, 3.56) | 1.36 (0.56, 3.31)       |

MMF: mycophenolate mofetil, CYC: cyclophosphamide, TAC: tacrolimus, GCs: glucocorticoids, all classes of GCs were converted to equivalent prednisone doses, HCQ: hydroxychloroquine, OR: odds ratio, CI: confidence interval, ROR is ratio of ORs. Multivariable analysis models were adjusted for gender (female = 1, male = 0), age (continuous), SLE disease period years (continuous), SLEDAI score on admission (continuous), hypertension (yes = 1, no = 0), diabetes mellitus (yes = 1, no = 0), mean daily prednisone equivalent dose (continuous), CYC treatment (yes = 1, no = 0), TAC treatment (yes = 1, no = 0), and other immunosuppressants (yes = 1, no = 0). <sup>a</sup> Other immunosuppressants including leflunomide, methotrexate, cyclosporin A, azathioprine, thalidomide and tripterygium glycosides.

**Supplementary Table 7. Joint effects of MMF and other major drugs on opportunistic infection of SLE patients.**

| Variables                                   | MMF | Opportunistic infection patients, n (%) (n = 163) | No infection patients, n (%) (n = 1762) | OR (95% CI)        | Adjusted OR (95% CI) |
|---------------------------------------------|-----|---------------------------------------------------|-----------------------------------------|--------------------|----------------------|
| <b>CYC</b>                                  |     |                                                   |                                         |                    |                      |
| No                                          | No  | 106 (6.6)                                         | 1490 (93.4)                             | 1.00               | 1.00                 |
| No                                          | Yes | 11 (11.6)                                         | 84 (88.4)                               | 1.84 (0.95, 3.56)  | 1.58 (0.79, 3.15)    |
| Yes                                         | No  | 26 (14.8)                                         | 150 (85.2)                              | 2.44 (1.54, 3.86)  | 1.70 (1.02, 2.82)    |
| Yes                                         | Yes | 20 (34.5)                                         | 38 (65.5)                               | 7.40 (4.16, 13.16) | 5.10 (2.67, 9.72)    |
|                                             | ROR |                                                   |                                         | 1.65 (0.64, 4.26)  | 1.91 (0.72, 5.06)    |
| <b>TAC</b>                                  |     |                                                   |                                         |                    |                      |
| No                                          | No  | 111 (7.1)                                         | 1449 (92.9)                             | 1.00               | 1.00                 |
| No                                          | Yes | 20 (19.0)                                         | 85 (81.0)                               | 3.07 (1.82, 5.19)  | 2.21 (1.25, 3.90)    |
| Yes                                         | No  | 21 (9.9)                                          | 191 (90.1)                              | 1.44 (0.88, 2.34)  | 1.21 (0.71, 2.03)    |
| Yes                                         | Yes | 11 (22.9)                                         | 37 (77.1)                               | 3.88 (1.93, 7.82)  | 2.38 (1.10, 5.12)    |
|                                             | ROR |                                                   |                                         | 0.88 (0.34, 2.31)  | 0.89 (0.33, 2.44)    |
| <b>Daily GCs</b>                            |     |                                                   |                                         |                    |                      |
| ≤ 20 mg                                     | No  | 56 (6.5)                                          | 804 (93.5)                              | 1.00               | 1.00                 |
| ≤ 20 mg                                     | Yes | 19 (18.4)                                         | 84 (81.6)                               | 3.25 (1.84, 5.72)  | 2.49 (1.36, 4.56)    |
| > 20 mg                                     | No  | 76 (8.3)                                          | 836 (91.7)                              | 1.31 (0.91, 1.87)  | 1.42 (0.97, 2.10)    |
| > 20 mg                                     | Yes | 12 (24.0)                                         | 38 (76.0)                               | 4.53 (2.24, 9.16)  | 2.69 (1.24, 5.85)    |
|                                             | ROR |                                                   |                                         | 1.07 (0.44, 2.61)  | 0.76 (0.30, 1.93)    |
| <b>HCQ</b>                                  |     |                                                   |                                         |                    |                      |
| Yes                                         | No  | 91 (7.3)                                          | 1157 (92.7)                             | 1.00               | 1.00                 |
| Yes                                         | Yes | 20 (18.3)                                         | 89 (81.7)                               | 2.86 (1.68, 4.85)  | 1.86 (1.04, 3.33)    |
| No                                          | No  | 41 (7.8)                                          | 483 (92.2)                              | 1.08 (0.74, 1.58)  | 1.11 (0.74, 1.66)    |
| No                                          | Yes | 11 (25.0)                                         | 33 (75.0)                               | 4.24 (2.07, 8.66)  | 3.04 (1.42, 6.51)    |
|                                             | ROR |                                                   |                                         | 1.37 (0.55, 3.45)  | 1.48 (0.56, 3.88)    |
| <b>Other immunosuppressants<sup>a</sup></b> |     |                                                   |                                         |                    |                      |
| No                                          | No  | 99 (6.6)                                          | 1408 (93.4)                             | 1.00               | 1.00                 |
| No                                          | Yes | 7 (8.6)                                           | 74 (91.4)                               | 1.35 (0.60, 3.00)  | 1.21 (0.53, 2.78)    |
| Yes                                         | No  | 33 (12.5)                                         | 232 (87.5)                              | 2.02 (1.33, 3.07)  | 1.56 (0.98, 2.49)    |
| Yes                                         | Yes | 24 (33.3)                                         | 48 (66.7)                               | 7.11 (4.18, 12.09) | 4.97 (2.70, 9.14)    |
|                                             | ROR |                                                   |                                         | 2.61 (0.95, 7.16)  | 2.62 (0.93, 7.37)    |

MMF: mycophenolate mofetil, CYC: cyclophosphamide, TAC: tacrolimus, GCs: glucocorticoids, all classes of GCs were converted to equivalent prednisone doses, HCQ: hydroxychloroquine, OR: odds ratio, CI: confidence interval, ROR is ratio of ORs. Multivariable analysis models were adjusted for gender (female = 1, male = 0), age (continuous), SLE disease period years (continuous), SLEDAI score on admission (continuous), hypertension (yes = 1, no = 0), diabetes mellitus (yes = 1, no = 0), mean daily prednisone equivalent dose (continuous), CYC treatment (yes = 1, no = 0), TAC treatment (yes = 1, no = 0), and other immunosuppressants (yes = 1, no = 0). <sup>a</sup> Other immunosuppressants including leflunomide, methotrexate, cyclosporin A, azathioprine, thalidomide and tripterygium glycosides.