Supplementary file part I

Supplementary Table 1 NPSLE syndromes according to 1999 ACR criteria of patients with SLE and neuropsychiatric symptoms attributed to SLE (NPSLE)

| NPSLE Syndrome                  | Inflammatory phenotype* | Ischemic phenotype |
|---------------------------------|-------------------------|--------------------|
|                                 | (n = 72)                | (n = 29)           |
| Aseptic meningitis              | 1 (1)                   | 0 (0)              |
| Cerebrovascular disease         | 20 (28)                 | 27 (93)            |
| Demyelinating syndrome          | 0 (0)                   | 0 (0)              |
| Headache                        | 7 (10)                  | 1 (3)              |
| Movement disorder (chorea)      | 3 (4)                   | 0 (0)              |
| Myelopathy                      | 7 (10)                  | 0 (0)              |
| Seizure disorders               | 6 (8)                   | 3 (10)             |
| Acute confusional state         | 7 (10)                  | 0 (0)              |
| Anxiety disorder                | 1 (1)                   | 0 (0)              |
| Cognitive dysfunction           | 33 (46)                 | 2 (7)              |
| Mood disorder                   | 12 (17)                 | 0 (0)              |
| Psychosis                       | 7 (10)                  | 0 (0)              |
| AIDP\(^b\)                      | 0 (0)                   | 0 (0)              |
| Autonomic disorder              | 0 (0)                   | 0 (0)              |
| Mononeuropathy                  | 0 (0)                   | 0 (0)              |
| Myasthenia gravis               | 0 (0)                   | 0 (0)              |
| Neuropathy, cranial             | 6 (8)                   | 0 (0)              |
| Plexopathy                      | 0 (0)                   | 0 (0)              |
| Polyneuropathy                  | 5 (7)                   | 0 (0)              |
| Other\(^c\)                     | 19 (26)                 | 0 (0)              |

Data is presented as n (%).

* Patients with NPSLE of inflammatory origin (n = 72): inflammatory or combined NPSLE phenotype.

\(^b\) Acute inflammatory demyelinating polyneuropathy.

\(^c\) Other NPSLE symptoms: cerebral vasculitis (n = 8), organic brain syndrome (n = 3), lethargy (n = 1) visual disturbance other than optic neuritis (n =1), apraxia (n =1), walking disorder (n =2), motor disorder left arm (n =1), paresis left arm and dysarthria (n = 1), increased intracranial pressure (n =1).
Supplementary file part II

Sensitivity analyses multiple imputation

A sensitivity analyses was performed with multiple imputation using chained equation (MICE) in STATA version 14.1. Sex, age, ACR criteria, disease duration, disease activity score (SLEDAI-2K), damage index (SDI), NPSLE and NPSLE phenotype and medication use were used for imputation (n = 50) using predictive mean matching.

**Supplementary Table 2** Result of sensitivity analysis using multiple imputation for the analysis of fatigue in patients with neuropsychiatric symptoms due to inflammation (inflammatory phenotype) and other causes (non-inflammatory phenotype)

| Phenotype                  | Inflammatory phenotype<sup>a</sup> | Inflammatory phenotype<sup>a</sup> | Non-inflammatory phenotype<sup>b</sup> | Non-inflammatory phenotype<sup>b</sup> |
|----------------------------|-----------------------------------|-----------------------------------|---------------------------------------|---------------------------------------|
|                            | Main analysis n = 81               | Main analysis n = 290             |                                       |                                       |
| **Fatigue (%)**            | 77.9                              | 78.5                              | 78.3                                  | 77.9                                  |
| **Extreme fatigue (%)**    | 50.0                              | 49.8                              | 46.3                                  | 45.8                                  |
| **SF-36 VT**<sup>**(mean, SE)**</sup> | 34.7                              | 34.3 ± 2.3                       | 34.5                                  | 34.3 ± 1.1                           |

**MFI (mean, SE)**

| Fatigue                  | 10.8                              | 10.8 ± 0.3                       | 11.3                                  | 11.3 ± 0.2                           |
| Physical Fatigue         | 11.5                              | 11.6 ± 0.3                       | 12.4                                  | 12.4 ± 0.2                           |
| Reduced Activity         | 9.8                               | 9.8 ± 0.5                        | 10.9                                  | 10.8 ± 0.2                           |
| Reduced Motivation       | 10.7                              | 10.8 ± 0.4                       | 11.3                                  | 11.3 ± 0.2                           |
| Mental Fatigue           | 9.6                               | 9.6 ± 0.4                        | 10.0                                  | 10.0 ± 0.2                           |
| Total score              | 52.2                              | 52.6 ± 1.4                       | 56.0                                  | 55.7 ± 0.6                           |
| **VAS (mean, SE)**       | 6.7                               | 6.8 ± 0.3                        | 7.6                                   | 7.6 ± 0.1                            |

<sup>a</sup>Patients with NPSLE of inflammatory origin: inflammatory or combined phenotype NPSLE.<br>
<sup>b</sup>Patients with non-inflammatory (NP)SLE: minor/non-NPSLE and ischemic NPSLE.

*MFI = multidimensional fatigue inventor, SE = standard error, SF-36 VT = Short-Form 36 Vitality Domain, VAS = visual analogue scale.*
**Supplementary Table 3** Sensitivity analyses studying the influence of the presence of neuropsychiatric symptoms due to inflammation (inflammatory phenotype) and other causes (non-inflammatory phenotype)

|                               | SF-36 VT | MFI total score | VAS       |
|-------------------------------|----------|-----------------|-----------|
|                               | β*       | 95% CI          | β         | 95% CI    | β         | 95% CI    |
| Inflammatory vs non-inflammatory (ref) (main result) | 0.9      | (-4.4; 6.1)     | -3.7      | (-6.8; -0.7) | -1.0      | (-1.7; -0.4) |
| Inflammatory vs non-inflammatory (ref) after multiple imputation | 0.1      | (-5.0; 4.8)     | -3.0      | (-5.8; -0.3) | -0.9      | (-1.5; -0.3) |
| Inflammatory vs minor/non-NPSLE (ref) (excluding ischemic NPSLE) | 1.4      | (-3.9; 6.6)     | -4.0      | (-7.1; -0.8) | -1.1      | (-1.7; -0.4) |
| Inflammatory vs non-inflammatory (ref) (excluding combined phenotype) | 2.0      | (-4.1; 8.0)     | -3.2      | (-6.8; 0.5)  | -0.9      | (-1.6; -0.1) |
| Inflammatory vs minor/non-NPSLE (ref) (excluding ischemic + combined) | 2.5      | (-3.5; 8.5)     | -3.4      | (-7.1; 0.3)  | -0.9      | (-1.7; -0.2) |
| NPSLE vs minor/non-NPSLE (ref) | 2.3      | (-2.4; 7.0)     | -3.4      | (-6.2; -0.7) | -0.9      | (-1.5; -0.3) |

* All β’s are corrected for age, sex and education.

*MFI = multidimensional fatigue inventory, SF-36 VT = Short-Form 36 Vitality Domain, VAS = visual analogue scale.*