**Supplementary Text**

*1.* ***Inclusion criteria***

1. Provision of written informed consent by subject.
2. Age ≥ 18.
3. Fulfill at least 4 of the American College of Rheumatology (ACR) classification criteria for SLE (25) for a minimum of 3 months prior to the first dose.
4. Active SLE disease defined by a Systemic Lupus Erythematosus Disease Activity index 2000 (SLEDAI-2k) (26) total score ≥6 or 1 system with a British Isles Lupus Assessment Group (BILAG) score of A or 2 systems with a BILAG score of B at screening (27).
5. Positive Antinuclear antibodies (ANA ≥1:80).
6. If using oral corticosteroids, patients must be receiving this medication for at least 6 weeks and on a stable dose of ≤40 mg/day of prednisone for at least 14 days before the first dose of the study medication.
7. If using antimalarial therapy (hydroxychloroquine or chloroquine), subjects must be taking this medication for ≥3 months and on stable dose for at least 4 weeks prior to the first administration of the study agent.
8. Women of childbearing potential must be willing to remain on a highly effective method of birth control during the study and 3 months after receiving the last study drug.

2. ***Exclusion criteria***

1. Inability or unwillingness to comply with the requirements of the protocol as determined by the investigator.
2. Pregnancy, breastfeeding, planning a pregnancy or use of a non-reliable method of contraception while enrolled in the study.
3. Known hypersensitivity or contraindication to MMF/EC-MPs or azathioprine (including known inherited thiopurine methyl-transferase (TPMT) severe deficiency).
4. Have received azathioprine or MMF/EC-MPs within the past 3 months prior to the first administration of the study agent.
5. Have received systemic immunosuppressive agents such as cyclosporine, methotrexate and leflunomide within the previous 3 months prior to the first study drug administration.
6. Have received cyclophosphamide within 3 months of starting screening.
7. Have an active lupus nephritis reported in recent biopsy and/or other assessments such as active urinary sediment, or end-stage renal disease, or severe or rapidly progressive glomerulonephritis.
8. Have received B cell depleting therapy (eg, Rituximab) within 12 months prior to the first study drug administration.
9. Have an active or a history of ongoing, chronic or recurrent disease including HIV and hepatitis B.
10. History of malignancy within 5 years before screening (with the exception of basal cell carcinoma treated by complete excision and with no evidence of recurrence for at least 3 months before the study agent administration and carcinoma in situ of the cervix that has been surgically cured).
11. Has any condition for which, in the opinion of the investigator participation would not be in the best interest of the patient.
12. Have a serious intercurrent illness that was likely to require additional systemic steroid therapy.
13. Have significant hematologic or laboratory abnormalities not attributed to SLE:

* Liver dysfunction (aspartate aminotransferase, alanine aminotransferase, or bilirubin greater than 2.5 times the upper limit of normal, measured on at least two separate occasions)
* Bone marrow insufficiency unrelated to active SLE (according to investigator judgment) with WBC <2500/mm3, absolute neutrophil count <1.3 x 103/μL, thrombocytopenia (platelet count) <50,000/mm3

1. Other medical condition that, in the investigator’s judgment, may be associated with increased risk to the subject or may interfere with study assessments or outcomes.
2. Have or had a substance abuse (drugs or alcohol) problem.

**3.** ***Adjustment of drug dose***

**AZA group**: Azathioprine will be started progressively to achieve a target dose of 2 mg / kg per day (given the impossibility of accurate dosing as the tablets are 50 mg) or according to the thiopurine methyltransferase (TPMT) levels and maintained for 6 months in the induction phase. After this time period, if clinical remission is achieved, the dose will be reduced progressively 25 mg (~0.5 mg/kg) every 3 months until their withdrawal if possible, always according to the medical judgment. The minimal duration of treatment in the mild/moderate flares will be 1 year and 2 for severe flares. In the event of relapse of the disease while reducing the dose no further reduction will be performed and the dose will be increased up to the previous dose if required to control the disease flare. If the drug had been withdrawn, in the event of clinical relapse, azathioprine will be re-started at the initial dose at the initial dose according to clinical judgment. Patients who were unable to tolerate the target dose or whose weight was below 50 Kg remained in the study if they tolerated a minimum dose of 50 mg of AZA per day during the first 6 months.

Dose adjustments:

1. If the white cell count was <3x109 cells/L, the azathioprine dose will be halved. When white cell count was <2x109 cells/L, azathioprine will be discontinued.

2. If ALT/AST were ≥5 times normal value azathioprine will be discontinued.

3. In the event of severe side effects (eg. Pancreatitis) azathioprine will be discontinued.

4. If patient suffered from severe infections, azathioprine will be discontinued; the continuation of AZA therapy was determined by the physician.

**Enteric-coated mycophenolate sodium** **group** (EC-MPS). EC-MPS will be started at a dose of 1440 mg/day according to gastrointestinal tolerance and sustained for 6 months the same dose. After this period of time if clinical remission has been achieved the dose will be progressively reduced, 360 mg / day every 3 months. Treatment will be withdrawn after at least 1 year of therapy in the mild/moderate initial flares and after 2 years for severe flares according to clinical judgment. In the event of relapse of the disease while reducing the dose no further reduction will be performed and the dose will be increased up to the previous dose if required to control the disease flare. If the drug had been withdrawn, in the event of clinical relapse, azathioprine will be re-started at the initial dose according to clinical judgment. Patients who were unable to tolerate the target dose remained in the study if they tolerated a minimum dose of 720 mg of EC-MPS per day during the first 6 months.

Dose adjustments:

1. If the white cell count was <3x109 cells/L, the EC-MPS dose was halved. When white cell count was <2x109 cells/L, EC-MPS was to be discontinued.

2. If the patient had obvious gastrointestinal symptoms, the dosage of EC-MPS could be decreased or EC-MPS could be taken after meals.

3. If patient suffered from severe infections, EC-MPS was to be discontinued, the continuation of EC-MPS therapy was determined by the physician.

***4. Concomitant medications***

Unnecessary changes were discouraged during the study.

**1. Corticosteroids:**

Changes were allowed according to the medical judgment.

If using oral corticosteroids, must be receiving this medication on a stable dose Prednisone dose from baseline is advised to be reduced progressively within the first 3 months after the first administration of the study agent according to clinical judgment.

Corticosteroid increments in the event of flare were as follow:

1. Mild/moderate flare: oral prednisone was to be increased up to a maxim dose of 0.5mg/kg and reduction was performed 5 mg/day every week to a maintenance dose of ≤7.5 mg/day.
2. Severe flare: Methylprednisolone pulses were allowed (1 gr/day x 3 days) followed by oral prednisone (1 mg/kg) tapering 10 mg weekly until a maintenance dose of ≤7.5 mg/day.

**2. Antimalarials**: It was recommended stable treatment dose through the study. According to medical judgment beyond week 24 it was permitted to adjust dosing of antimalarials.

**3**. **Nonsteroidal anti-inflammatory drugs (NSAIDS):** NSAIDS and other analgesics were prescribed at the marketed approved doses and had to remained stable at least 2 weeks prior to the first study agent dose and though week 12. Addition of new NSAIDS was not permitted for the treatment of lupus-related disease. After week 12 adjustments in NSAIDs therapy were allowed.

**4.** Drugs which can affect the azathioprine metabolism were forbidden (eg, Allopurinol)

**5. Prohibited rescue therapies**

1. Biologic agents targeted at reducing TNFα (including but not limited to infliximab, golimumab, etanercept and adalimumab)

2. B-cell depleting agents (anti-CD20 [eg, Rituximab]

3. Interleukin-1 inhibitors (eg, Anakinra)

4. Calcineurin agents (eg, Tacrolimus, cyclosporine A)

5. Cytotoxic drugs such as cyclophosphamide

6. Thalidomide/ Lenalidomide

7. Pulses of Methylprednisolone (1000 mg iv x 3 days)

***6. Patient withdrawal***

Subjects may withdraw from the protocol at any time without any reason. In addition, patients would be withdrawn for any of the following reasons:

* Lost of follow up or death
* Withdrawal of informed consent
* Lack of adherence with the protocol
* Development of a renal flare
* Lack of efficacy after at least 3 months of therapy
* Aggravation of SLE or the need for any forbidden immunosuppressant such as cyclophosphamide, IV immunoglobulins or anti-CD20 therapy.