Model Name
Lupus, Systemic Lupus Erythematosus (SLE)

Item Number
558000

Introduction
Systemic lupus erythematosus (SLE) is an autoimmune disease that is characterized by auto antibody production. It involves many organs such as skin, joints, kidneys and the central nervous system (CNS). The renal disease (lupus nephritis) is considered the most severe manifestation of SLE with an increased risk of morbidity and mortality.

The best characterized mouse model of SLE is the NZB/W F1 model. NZBWF1/J hybrids develop lupus-like autoimmunity characterized by immunoglobulin G auto antibody production and progressive severe glomerulonephritis that closely resembles human SLE. The NZBWF1/J mouse model has been used extensively to study the mechanisms of SLE and evaluate the therapeutic efficacy of drug candidates.

Procedure Summary
Female NZBWF1/J mice of 24-26 weeks of age are used in the study. The urine is screened three times per week for proteinuria, and the level of proteinuria is graded according to the manufacture’s instruction. Mice are randomly assigned to different treatment groups each with 10 animals based on the level of proteinuria as well as the body weight after there is kidney damage (glomerulonephritis) as evidenced by the presence of proteinuria of ≥30 mg/dl on two occasions two days apart at around 26-28 weeks of age.

After kidney damage, vehicle and test articles are administered orally once daily (QD) for 12 weeks. The positive control consists of methylprednisolone (MP) and cyclophosphamide (CTX). MP is given orally at 2 mg/kg once a day for 6 weeks followed by 1 mg/kg once a day for another 6 weeks. CTX is given orally at 6 mg/kg once a day for 12 weeks. Body weight and proteinuria are recorded once a week, mortality is observed once daily.

Blood is collected before dosing (the actual timing may vary) and every 4 weeks thereafter. Serum is processed for measuring serum blood urea nitrogen (BUN), creatinine by optimized UV method with an automatic analyser and for the detection of titers of total IgG and anti-dsDNA autoantibodies by ELISA.

The animals are sacrificed at the end of week 38 or 40, and kidneys, spleen and draining lymph nodes are collected and weighed (optional). Kidneys are paraffin embedded and stained with hematoxylin and eosin for histopathology (optional).

Data are expressed as a mean ± SEM. Two-way ANOVA followed by Bonferroni’s test is applied for comparison between vehicle and treated groups. p<0.05 is considered significant.

Suggested Testing
• n=10/group (study design dependent)
• Doses may be administered TOP, PO, IV, IP, and SC
• Assessments available: Blood chemistry, total IgG and anti-dsDNA antibodies, biomarker analysis (protein or mRNA), organ weight (kidney, spleen) and Histopathology

Turnaround Time(s)
• Acute Assay: In-Life completion in 16-18 weeks from sample receipt
• For Subacute Assays: 6 weeks to 3 months
Literature

Modified Protocols
We will readily accommodate client-specified alterations.

Laboratory
These assays are performed at our AAALAC accredited laboratory in Taipei.

Animal Welfare
All aspects of this work are performed in general accordance with the Guide for the Care and Use of laboratory animals (National Academy Press, Washington, DC, 2011). The study protocol was approved by the Pharmacology Discovery Services IACUC and is performed with the oversight of veterinarians to assure the humane treatment of laboratory animals.

Reference Compounds
Methylprednisolone (MP) + Cyclophosphamide (CTX)

Last modified September 18, 2019