Mouse Models of Systemic Lupus Erythematosus (SLE)

NZB/W F1 Mouse Model of SLE

Characteristics:

- The most commonly used preclinical model for SLE.
- Mouse model was originally developed by Helyer at Howie in 1963 and subsequently transferred to Jackson Laboratories.
- Develops anti-dsDNA (auto) antibodies at ≥ 16 weeks of age.
- Develops 3+ proteinuria after 20 weeks of age.
- NZM lines: genetic susceptibility loci (*sle1,2,3*)

Clinical Measures:

- Proteinuria
- Weekly Body Weights
- Anti-dsDNA antibody ELISA
- Glomerular Filtration Rate
- IDEXX clinical analyzer

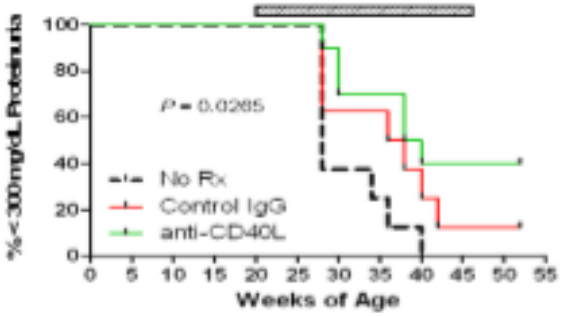
Additional Readouts:

Flow Cytometry:
B cells, T cells, dendritic cells, NK cells, NKT cells, apoptosis. Experienced with multicolor (up to 4-5 color) panel design and validation with human (PMBCs), and rat and mouse (whole blood, splenocytes, lymph node cells) cells

Histopathology:
glomerulonephropathy, dilated tubules, degenerate tubules, lymphocyte aggregates

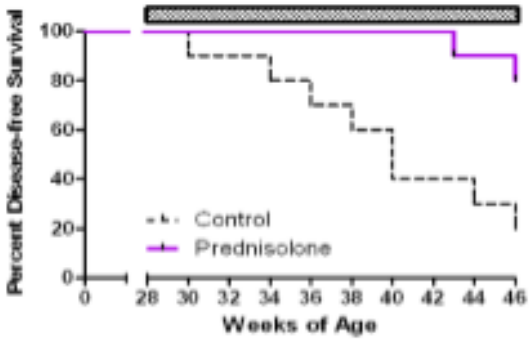
NZB/W F1 SLE Mouse Prevention Study

- N=10/group with proteinuria = 0+ at 20 weeks of age
- Dose once every two weeks from 20 - 46 weeks of age
- Measure body weights once weekly and proteinuria once every two weeks.
- Humane survival end points: ≥ 3+ proteinuria on two consecutive weeks

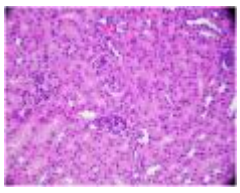


NZB/W F1 SLE Mouse Remission Study

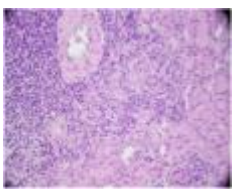
- NZB/W F1 female mice with moderate proteinuria (1 - 2+) were entered into groups at 28 weeks of age (n = 10/group) and initiated treatment (bar).
- Proteinuria was measured once every two weeks (the following week to confirm a ≥ 3+ reading).
- Humane survival end points: ≥ 3+ proteinuria on two consecutive weeks.



NZB/W F1
Proteinuria = 3+ at 46 weeks of age



MRL/lpr
Proteinuria = 3+ at 15 weeks of age



Both mice reached the same humane endpoint, but lymphocyte aggregates were noticeably more severe in MRL/lpr mice (mean score = 3) compared to NZB/W F1 mice (mean score = 2)