the importance of remaining vigilant about nephritis risk in patients of diverse demographics five years and more after diagnosis with SLE.

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22  BARICITINIB INHIBITS B CELL ACTIVATION AND AMELIORATES MURINE LUPUS

Abstract 22 Figure 1 Effects of baricitinib treatment on lupus-prone mice. Baricitinib treatment showed improvements such as reduction of skin ulcers and attenuation in mortality and an imbalance in ROS production may lead to oxidative stress, mitochondrial lipid, protein and DNA modifications, and alterations in the production of adenosine triphosphate (ATP). Baricitinib is a coenzyme Q10 synthetic analog with antioxidant properties previously tested in humans to treat different diseases where mitochondrial function is compromised. This study aimed to assess if idebenone mitigates murine lupus.

Methods Two different doses of idebenone were given orally to MRL/lpr mice for 8 weeks. At euthanasia, treated and untreated mice were analyzed and compared for clinical, immunologic and metabolic parameters including autoantibody generation, proteinuria, kidney function and pathology, renal immune complex deposition, endothelium-dependent vasorelaxation, assessment of pro-inflammatory gene expression, quantification and characterization of neutrophil extracellular trap (NET) formation and mitochondrial ROS, measurement of complex II-specific activity and cardiac lipid peroxidation.

Results Idebenone was well tolerated and led to significant attenuation in mortality and an improvement of glomerular inflammation, renal function, skin ulcers and splenomegaly. The levels of proinflammatory cytokines and inflammasome-related genes were significantly decreased by idebenone. In addition, we observed inhibition of NET formation both in lupus mice bone marrow neutrophils and in neutrophils from lupus patients. Enhanced complex II-specific activity and mitochondrial function were shown in cells isolated from idebenone-treated lupus-prone mice, suggesting improved mitochondrial function and reduction of oxidative stress. Idebenone-treated mice also displayed reduced heart lipid peroxidation.

Conclusions Idebenone improves murine lupus. These results suggest that idebenone and other drugs that improve mitochondrial function may have a therapeutic role in SLE.

Funding Source(s): This study was supported by the Intramural Research Program, NIAMS/NIH (ZIA AR041199) and the Alliance for Lupus Research.

23  TREATING LUPUS-PRONE MICE WITH A COENZYME Q10 ANALOG DECREASES DISEASE PARAMETERS INDICATING A THERAPEUTIC ROLE IN SYSTEMIC LUPUS ERYTHEMATOSUS
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Abstract 23 Figure 1 Effects of idebenone treatment on lupus-prone mice. Idebenone treatment showed improvements such as reduction of skin ulcers and attenuation in mortality and an imbalance in ROS production may lead to oxidative stress, mitochondrial lipid, protein and DNA modifications, and alterations in the production of adenosine triphosphate (ATP). Idebenone is a coenzyme Q10 synthetic analog with antioxidant properties previously tested in humans to treat different diseases where mitochondrial function is compromised. This study aimed to assess if idebenone mitigates murine lupus.

Methods Two different doses of idebenone were given orally to MRL/lpr mice for 8 weeks. At euthanasia, treated and untreated mice were analyzed and compared for clinical, immunologic and metabolic parameters including autoantibody generation, proteinuria, kidney function and pathology, renal immune complex deposition, endothelium-dependent vasorelaxation, assessment of pro-inflammatory gene expression, quantification and characterization of neutrophil extracellular trap (NET) formation and mitochondrial ROS, measurement of complex II-specific activity and cardiac lipid peroxidation.

Results Idebenone was well tolerated and led to significant attenuation in mortality and an improvement of glomerular inflammation, renal function, skin ulcers and splenomegaly. The levels of proinflammatory cytokines and inflammasome-related genes were significantly decreased by idebenone. In addition, we observed inhibition of NET formation both in lupus mice bone marrow neutrophils and in neutrophils from lupus patients. Enhanced complex II-specific activity and mitochondrial function were shown in cells isolated from idebenone-treated lupus-prone mice, suggesting improved mitochondrial function and reduction of oxidative stress. Idebenone-treated mice also displayed reduced heart lipid peroxidation.

Conclusions Idebenone improves murine lupus. These results suggest that idebenone and other drugs that improve mitochondrial function may have a therapeutic role in SLE.

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