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PRECLINICAL AND CLINICAL CHARACTERIZATION OF CENERIMOD, A POTENT, SELECTIVE, AND ORALLY ACTIVE SPHINGOSINE-1-PHOSPHATE RECEPTOR 1 MODULATOR IN SLE

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Background Reported here is the characterization of cenerimod, a novel, potent, selective, and orally active sphingosine-1-phosphate receptor 1 (S1P₁) modulator in the context of SLE.

Methods Lymphocytes from patients with SLE and healthy subjects were assessed for cenerimod-induced S1P₁ receptor internalization. Efficacy of cenerimod was evaluated in the MRL/lpr lupus mouse model. In a 12-week phase 2 clinical trial in SLE subjects treated with multiple doses of cenerimod (NCT02472795), lymphocyte subsets and inflammatory biomarkers were characterized.

Results Cenerimod was potent and efficacious at inducing S1P₁ receptor internalization in T and B lymphocytes with an EC₅₀ of ~15 nM in both healthy subjects and patients with SLE. In lupus-like MRL/lpr mice treated with cenerimod, circulating T and B lymphocytes were reduced, which resulted in reduced immune infiltrates into tissue, reduced autoantibody production and inflammation, preserved organ function, and increased survival. In SLE subjects treated with cenerimod for 12 weeks, a dose-dependent reduction of circulating T cells (95%), B cells (90%), and antibody-secreting cells (85%) was evident. Furthermore, a reduction in anti-dsDNA antibodies and IFN- α , two key inflammatory molecules, was observed.

Conclusion Cenerimod was potent and efficacious in reducing S1P₁ receptor surface expression on lymphocytes, resulting in reduced circulating T and B lymphocyte populations, including antibody-secreting cells, and a decrease in inflammatory biomarkers in SLE subjects. Furthermore, cenerimod significantly ameliorated systemic and organ-specific autoimmunity in a mouse model of SLE. These results warranted the further investigation of the clinical efficacy and safety of cenerimod in the ongoing phase 2b clinical trial (NCT03742037).

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Poster presentations

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ANTIPHOSPHOLIPID SYNDROME IN QATAR: EPIDEMIOLOGICAL, CLINICAL, AND IMMUNOLOGICAL CHARACTERISTICS

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Purpose The aim of this study is to analyze epidemiological, clinical, and immunologic characteristics of primary and secondary antiphospholipid syndrome (APS) cases in Qatar.

Methods All patients with primary and secondary APS attending rheumatology clinics from January 2017 to May 2019 at Hamad General Hospital were identified and medical records were retrospectively reviewed.

Results 131 patients with APS who fulfilled revised Sapporo APS classification criteria were included- 116 women (88.5%) and 15 men (11.5%). 79 patients (60.3%) had primary and 52 patients (39.7%) had secondary APS. 41 patients (31.3%) had thrombotic event only, 64 patients (48.9%) had pregnancy morbidity only, and 26 patients (19.8%) had both thrombosis as well as pregnancy morbidity. 7 patients (5.4%) had arterial thrombosis only, 48 patients (36.6%) had venous thrombosis only and 12 patients (9.1%) had both arterial and venous thrombosis. 103 (78.6%) patients had pregnancy morbidity out of the 116 female patients. Early fetal loss was the commonest pregnancy morbidity seen in 73 patients (70.9%), followed by late fetal loss in 57 patients (55.3%).

48 patients (36.6%) had aCL IgG positive and 15 patients (11.5%) had aCL IgM positive, either one was positive in 54 patients (41.2%). 42 patients (32.1%) had B2GP IgG positive and 19 patients (14.5%) had B2GP IgM positive, either one was positive in 53 patients (40.7%). LA was positive in 121 patients (92.4%). There were 71 patients (54.2%) with single positive aPL test, 21 patients (16%) with double positive and 37 patients (28.2%) with triple positive aPL test results. LA was the most common single positive aPL test, seen in 65 patients (50.3%).

Conclusion The clinical manifestation and immunological characteristics of patients with APS in Qatar are diverse. Our cohort has much higher prevalence of LA positivity compared to other cohorts around the world. We also have a higher incidence of pregnancy morbidities.

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DIFFICULTIES IN MANAGING A PATIENT WITH MULTI-ORGAN DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND A HIGH RISK OF THROMBOTIC EVENTS IN ANTIPHOSPHOLIPID SYNDROME (CASE REPORT)

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Background Systemic lupus erythematosus (SLE) is a multisystem disease with many clinical manifestations. Late diagnosis, kidney damage, neuropsychiatric disorders, high risk of thrombotic events, resistance to therapy worsen the prognosis of the disease and increase mortality.

Methods Description of a clinical case of multiple organ damages in a patient with SLE and concomitant antiphospholipid syndrome (APS).

Results We describe a case report of organ damage in a patient with SLE and concomitant APS. The clinical and laboratory manifestations for the entire period of the disease are given below (table 1). Now the main manifestation of the disease in