Abstract 227 Figure 1 Distribution of Lupus Severity Index in all Patients and in different ethnic groups

We investigated the performance and characteristics of the LSI in a large multiethnic lupus cohort.

Methods Patients from a single academic center were followed from 1990–2016 using a custom database. Records of all SLE patients were abstracted. Variables included birthdate, diagnosis date, ethnicity, ACRc, SLICC Damage Index (SDI), treatment and date of death. Ethnicity was categorized into White (WHI), Asian (ASN), Indigenous (IND), and Other. The LSI was calculated from ACRc, and compared between ethnicities and demographic variables known to be associated with severe SLE using t-tests, ANOVA, Pearson correlation coefficient and logistic regression.

Results 832 SLE patients were identified: 497 (60%) WHI; 220 (26%) IND; 91 (11%) ASN; 24 (3%) Other. Mean age was 49 years, mean disease duration 15 years, 90% female, mean age at diagnosis 35; 163 (20%) of patients had died. The mean LSI was 6.9, range 3.2–9.7. The distribution of the LSI was similar to that in the original dataset (figure 1A) and the area under the ROC curve, measured against prescription of major immunosuppressive drugs, was 0.69 (95% CI 0.65–0.73). LSI was higher in males compared to females (7.3 vs. 6.9; $p=0.019$), and was negatively associated with onset age (Onset <18 years LSI=7.8; 18–50 years LSI=6.8; >50 years LSI=6.6; $p<0.001$). LSI correlated with SDI (Pearson 0.28, $p<0.001$), and was a predictor of accruing any damage (SDI>1) (OR 1.2 95% CI 1.1–1.3). LSI was higher in non-whites compared to whites: WHI LSI=6.6; IND LSI=7.2; Other LSI=7.3; ASN LSI 8.1; $p<0.001$). LSI was a predictor of early mortality (Death at age <50, or disease duration <10 years): OR 1.2; 95% CI 1.0–1.3). The distribution of the LSI varied by ethnic group with more uniformly severe disease in ASN patients (figure 1B, C) compared to WHI and IND.

Conclusions Similar to the original publication, higher LSI correlated with male sex, younger onset age, and non-white ethnicity; all groups shown to have more severe SLE. LSI was also a predictor of damage and early mortality. In addition we also found the distribution of LSI to differ between ethnicities. These findings confirm the utility of the LSI in stratifying patients by severity, and supports further exploration of the LSI to investigate contributors to severe SLE.

REFERENCE

1. Bello GA et al. *Lupus Science & Medicine* 2016.

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VERDINEXOR, AN INHIBITOR OF THE NUCLEAR EXPORT PROTEIN EXPORTIN-1 PREVENTS LUPUS PROGRESSION BY LIMITING GERMINAL CENTER FORMATION AND DEVELOPMENT OF AUTOREACTIVE ANTIBODY SECRETING CELLS

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Background Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by simultaneous activation of the innate and adaptive arms of the immune system. Recently, the nuclear export protein exportin-1 (XPO1) has surfaced as an attractive target for the treatment of SLE. Selective Inhibitor of Nuclear Export (SINE) compounds such as verdinexor (KPT-335) are potent, orally available XPO1 inhibitors. SINE compounds inhibit the nuclear export of over 220 cargoes, and this pleiotropic effect on multiple signaling pathways exerts apoptotic and anti-inflammatory effects, particularly in dampening NF- κ B transcriptional activity. Based on previous studies with SINE compounds, we sought to define the minimal amount and frequency of verdinexor treatment necessary to maintain disease inhibition.

Methods To evaluate the minimal efficacious dose of verdinexor in SLE, cohorts of mice with established disease were dosed orally twice weekly with 7.5 mg/kg verdinexor or vehicle for eight weeks. Thereafter, various administration schedules of verdinexor (7.5 mg/kg) plus or minus bortezomib (0.75 mg/kg) a proteasome inhibitor (PI) known to eliminate autoreactive antibody-secreting cells (ASC) were administered for 4 weeks to examine their ability to control recurrent disease. We used flow cytometry and ELISPOT to enumerate ASC in the spleen and bone marrow (BM) and immunofluorescence to visualize germinal centers (GC) in spleen.

Results Therapy with verdinexor twice weekly significantly inhibited disease progression (GC: Control=622499.06 338011.04 vs KPT-335=100952.44 62652.09, $p=0.0033$. plasmablasts: Control=263790.82 148146.57 vs KPT-335=20967.31 19009.25, $p=0.0027$. plasma cells: Control=62078.36 22539.49 vs KPT-335=21277.82 13909.45, $p=0.0056$). Thus, we observed significantly decreased levels of GC B cells, plasma cells and plasmablasts in the BM and the

spleen with 4 weeks of induction therapy. The potent effect of SINE compound monotherapy on GC and auto-reactive ASC was further highlighted by the pronounced elimination of GCs histologically and reduction in auto-reactive ASC achieved after 4 weeks of maintenance therapy administered once weekly. In a concurrent study, when combined with bortezomib, 1 week verdinexor plus PI treatment resulted in a synergistic effect, significantly reducing in the number of auto-reactive ASC, particularly in the BM.

Conclusions Verdinexor has demonstrated efficacy by reducing generation and survival of auto-reactive immune cells. Additional experiments are underway to examine if inhibition of the canonical NFB pathway underlies verdinexors inhibitory effect. Together, our findings suggest the potential of SINE compounds to have a significant impact on SLE disease progression alone or in combination with currently utilized PIs.

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229 CLINICAL CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS WITH MALIGNANT TUMORS

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Background Rheumatic disease is caused by immune abnormality, which results in the immune response of the body to auto-antigens and causes tissue damage. The immune system eliminates or inhibits the growth of tumor cells through various ways. When the immune function abnormality leads to the escape of immune surveillance of tumor cells, it can lead to tumorigenesis. The risk of malignant tumors is higher than ordinary people in systemic lupus erythematosus (SLE) patients, which were mainly hematological tumors, especially non-Hodgkin lymphoma. The risk of Hodgkin lymphoma, leukemia and multiple myeloma was also increased, which was associated with BAFF changes, APRIL signal transduction, increased IL-6 activity and EB virus infection. Increased risk of malignant tumors in SLE patients, including lung cancer, hepatobiliary cancer, thyroid cancer, vulvar/vaginal malignancies and cervical dysplasia, was also reported, which was associated with SLE disease activity in specific organs, inflammatory stimulation, oxidative damage, changes in viral clearance and/or specific drug use.

Methods Twenty SLE patients with malignant tumors admitted to the General Hospital of Ningxia Medical University from October 2008 to October 2018 were selected. Their sex, age, time of diagnosis of rheumatism and tumors, types of tumors, clinical stages and prognosis were summarized and analyzed.

Results Malignant tumors occurred in 20 (0.50%) of 3970 SLE patients, the average age was 54.43 ± 7.95 . There were 4 cases of lung cancer, 3 cases of non-Hodgkin lymphoma and liver cancer, 2 cases of thyroid cancer, uterine cancer and skin cancer. Multiple myeloma, gastric cancer, pancreatic cancer and nasopharyngeal carcinoma were found in 1 case respectively. The median course of malignant tumors in SLE patients was 3.42 years. 79.41% of the patients were diagnosed before tumors, 16.35% of the cases occurred at the same time, and only 4.24% of tumors were diagnosed before SLE. Phase IV was the most common clinical stage in the diagnosis of tumors, accounting for 59.74%. In SLE

patients with tumors, the survival time ranged from 1 month to 39 months, with a median survival time of 9.2 months.

Conclusions Most malignant tumors are found after SLE diagnosis, with a median course of 3.42 years, and occur more frequently between the ages of 50 and 60. SLE may be associated with various types of malignant tumors, lung cancer, non-Hodgkin's lymphoma and liver cancer were the most common tumors, and the clinical staging of tumors is late and the prognosis is poor, with the median survival time is 9.2 months.

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230 SYSTEMIC LUPUS ERYTHEMATOSUS AND RAPIDLY PROGRESSIVE CARDIOGENIC SHOCK

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Background Symptomatic lupus myocarditis is a rare but life-threatening complication of systemic lupus erythematosus (SLE). Clinical manifestation is variable and includes dyspnea, chest pain, peripheral edema, fever, nausea, vomiting, or palpitations. We describe a case of a young female who developed rapid progressive cardiogenic shock secondary to lupus myocarditis.

Methods Not applicable as it is a clinical vignette.

The abstract for clinical vignette is attached as a separate document

Results Not applicable as it is a clinical vignette

The abstract for clinical vignette is attached as a separate document

Conclusions The diagnosis of lupus myocarditis is usually achieved clinically and with the use of TTE, cardiac MRI or biopsy. However, none of the current diagnostic modalities have established sensitivity or specificity. Our patient only developed significant TTE findings during the late stage, which led to an unfortunate delay in diagnosis. We suggest that physicians should always have a broad differential diagnosis and high clinical suspicion to avoid late diagnosis and mismanagement of patients, especially when dealing with cardiac manifestations of SLE.

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231 tRNA DERIVED FRAGMENTS (tRFs) REGULATE OXIDATIVE PHOSPHORYLATION TO PARTICIPATE IN SLE PATHOGENESIS

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Background tRNA derived fragments (tRFs) are 18 to 40-nucleotide (nt) small RNAs cleaved from mature tRNAs or precursor tRNA transcripts. There is growing evidence that tRFs play important roles in cellular homeostasis. This study focused on abnormal expression of tRFs in CD4⁺T lymphocytes from SLE patients, their function on