

Conclusions ANA IIF alone rare and patients infrequently develop nephritis, leucopenia, lymphocytopenia, AITP, AIHA. In patients ANA IIF alone attribution of ACR/SLICC clinical criteria needs to be point of emphasis and unless biopsy proven, alternative explanation for proteinuria should be considered. Data argues inclusion criteria for clinical trials, rather than allowing ANA IIF alone or dsDNA, may need to require ANA IIF and at least one of the following (dsDNA, Sm, Ro, La, aPL, or hypocomplementemia) to avoid enrolling patients that do not have SLE.

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65

INCREASED WORK LOSS DURING PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS COMPARED TO MATCHED HEALTHY CONTROLS

¹Birgit S Blomjous, ²Marieke M ter Wee, ¹Alexandre E Voskuyl, ³Johanna IP de Vries, ¹Irene EM Bultink*. ¹Department of Rheumatology, Amsterdam Rheumatology and immunology Center, Amsterdam UMC, location VUmc, Amsterdam, Netherlands; ²Department of Epidemiology and Biostatistics, Amsterdam UMC, location VUmc, Amsterdam, Netherlands; ³Department of Obstetrics and Gynecology, Amsterdam UMC, location VUmc, Amsterdam, Netherlands

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Background Women with systemic lupus erythematosus (SLE) might be more vulnerable to reduce or stop working during pregnancy because of the increased risk of pregnancy complications compared to the general population. However, no data on work loss during pregnancy and return to work after maternity leave in patients with SLE are available. We aimed to investigate several work outcomes during and after pregnancy in women with SLE compared to matched pregnant controls.

Methods A case-control study on employment was performed in pregnant women with SLE and matched controls. Matching criteria were age, year of delivery, and number of living infants. Employment was defined as having 8 hours/week of paid work before conception. Four work outcomes were investigated: interruption of work for >1 week during pregnancy, complete cessation of work during pregnancy for >1 week until delivery, reduction in working hours during pregnancy, and the time in weeks to return to work after maternity leave.

Results A total of 42 women were included (21 SLE patients, 21 controls). Mean SELENA-SLEDAI before pregnancy in SLE patients was 2.6 (SD 2.3). Interruption of work for >1 week or completely stop working during pregnancy occurred in 10 women with SLE compared to 2 controls (OR=8.6, 95% CI [1.6–46.8], $p=0.012$). From the women who completely stopped working until delivery ($n=8$), 7 women had SLE versus 1 control (OR=1.4, 95% CI [0.07–28.1], $p=0.826$). In addition, in women continuing work, reduction of working hours during pregnancy occurred in 5 women with SLE versus 3 controls (OR=1.9, 95% CI [0.4–9.1], $p=0.436$).

After delivery, the median (IQR) duration of return to work after maternity leave was 4 (0–6.8) weeks after maternity leave for women with SLE and 2 (0–4) weeks later for controls (Mann-Whitney U test, $p=0.977$). No difference in number of women with delay of return to work after maternity leave (yes/no) was found between women with SLE and controls ($n=9$ versus $n=11$, respectively, OR=1.0, 95% CI [0.3–3.7], $p=0.973$).

Conclusions Pregnant women with SLE more frequently completely stop working or reduce working hours compared to matched healthy controls. These findings warrant improved counseling of these women and attention of health care providers, including company doctors.

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66

NEUROLOGIC MANIFESTATIONS OF THE ANTIPHOSPHOLIPID SYNDROME AND RESPONSE TO HYDROXYCHLOROQUINE: A DESCRIPTIVE STUDY

¹Nahia Plaza Aulestia*, ¹Consuelo Ramos Giráldez, ¹José Luis Marengo de la Fuente, ²Mercedes Romera Tellado. ¹Valme Hospital (Rheumatology unit); ²Valme Hospital (Neurology unit)

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Background The primary antiphospholipid syndrome (APS) is characterized by arterial and/or venous thrombosis and pregnancy morbidity in the presence of anticardiolipin antibodies (aCL) and/or lupus anticoagulant (LA). In addition to prothrombotic effects of aPL on the brain, there are immunologic effects with proof of direct binding of aPL to various types of brain cells, presented as cognitive dysfunction (CD), migraine, seizure, multiple sclerosis-like syndrome (MS-like), transverse myelitis (TM), movement disorders, or psychiatric symptoms.

Methods We examined 3 patients who were diagnosed primary APS. The patients were assessed with careful history taking, physical examination, blood laboratory evaluation, and MRI or head-CT. Our main objective was to describe neurologic manifestations of APS in our patients at Valme University Hospital and the response to treatment with hydroxychloroquine

Results Among the 3 patients, there was male preponderance with 3 men and no-women. The mean age of presentation was 33.66 ± 5.2 years (range, 23–50 years) and with a current mean age of 37 ± 14.93 years. There was no mortality in our series. One of them debuted with sudden loss of consciousness along with jaw stiffness and posterior amnesia. The other one presented pricking sensation and involuntary movement of his right upper limb extending to right lower limbs without posterior generalization, and the third patient consulted with frontal, pulsating headache and binocular diplopia. 100% were LA positive with prolonged Activated Partial Thromboplastin Time and dilute Russell viper venom time and negative for ANA with no collagenosis sign or symptoms. Neither presented complement alteration or cerebrospinal fluid variation. We observed positivity for aCL in one patient (33%). In 2 of 3 patients (66.66%), cortico-subcortical space occupant lesions (SOL) were observed, some of them with contrast enhancement, mimicking demyelinating lesion, while the other patient didn't present any abnormality in the MRI images. All patients presented an appropriate response to treatment with prednisone, in downward treatment regimen, aspirin and hydroxychloroquine 200 mg twice a day. At the four-year follow-up, all of them remain asymptomatic. We observed a lessening of SOL in MRI images due to the treatment in two patients but the third one presented new lesions due to suspension of prednisone, which was reintroduced, lessening of SOL.

Conclusions The neurological affection presented in APS can mimic multiple sclerosis symptoms and it is difficult to differentiate both entities. That is why aPL determination should be part of screening tests and should not be delayed if the

diagnosis of APS is suspected. Hydroxychloroquine could be a valid treatment in CNS manifestations in patients with APS

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67 THERAPEUTIC AND RENAL PROTECTIVE EFFECTS OF DZ2002, A REVERSIBLE SAHH INHIBITOR, ON LUPUS-PRONE NZB×NZW F1 MICE

¹Shijun He*, ¹Zemin Lin, ²Wei Tang, ¹Jianping Zuo. ¹Shanghai Institute of Materia Medica, Chinese Academy of Sciences; ²Shanghai Institute of Materia Medica

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Background Glomerulonephritis is one of the major complications and causes of death in systemic lupus erythematosus (SLE). DZ2002 is a reversible S-adenosyl-l-homocysteine hydrolase (SAHH) inhibitor with potent therapeutic activity against lupus nephritis in mice. However, the molecular events underlying the renal protective effects of DZ2002 remained unclear. This study is designed to uncover the molecular mechanisms of DZ2002 on glomerulonephritis of lupus-prone mice.

Methods Female NZB/W F1 mice were treated orally with DZ2002, and the proteinuria level and body weight were monitored. After the mice were euthanized, serum biochemical parameters and renal damage were determined. Splenocytes of NZB/W F1 mice were isolated for *ex vivo* study. Toll-like receptor (TLR)-stimulated murine bone marrow-derived dendritic cells (BMDCs) were used for *in vitro* study. The LC-MS-based label-free quantitative (LFQ) proteomic approach was applied to analyze the kidney tissue samples from the NZB/W F1 mice treated with DZ2002 or vehicle. KEGG pathway enrichment and direct protein-protein interaction (PPI) network analyses were used to map the pathways in which the significantly changed proteins (SCPs) involved. The selected proteins from proteomic analysis were validated by Western blot analysis and immunohistochemistry in the kidney tissues.

Results Treatment of the mice with DZ2002 significantly attenuated the progression of glomerulonephritis and improved the overall health. The improvement was accompanied by decreased levels of nephritogenic anti-dsDNA antibodies, serum IL-17, IL-23p19 and TGF-. DZ2002 also significantly suppressed TLR agonists-stimulated up-regulation in IL-6 and IL-23p19 production in murine BMDCs, and prevented Th17 differentiation and suppressed IL-17 secretion by the T cells in a BMDC-T cell co-culture system. Pathway analysis of proteomic data revealed that 13 SCPs were involved in tight junction and focal adhesion process. Further protein expression validation demonstrated that DZ2002 treated NZB/W F1 mice exhibited down-regulation of -actinin-4 and integrin-linked kinase (ILK), as well as the restoration of 1-integrin activation in kidney tissues compare with vehicle treated ones.

Conclusions Our study demonstrated that DZ2002 effectively ameliorates lupus syndrome in NZB/W F1 mice by regulating TLR signaling-mediated antigen presenting cell (APC) responses. Alongside of attenuating glomerular immune complexes deposition and impeding pathologic lymphocytes polarization in SLE, the renal protective effects of DZ2002 may partly attributed to stabilization of the actin cytoskeleton and maintenance of podocyte numbers, in turn, are effective to improve proteinuria and kidney function in lupus nephritis.

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68 ADMINISTRATION OF ARTEMISININ ANALOGUE SM934 AMELIORATES DISEASE MANIFESTATION IN LUPUS-PRONE MICE VIA RESTORING IMMUNE HOMEOSTASIS

¹Zemin Lin*, ¹Jianping Zuo, ¹Shijun He, ²Wei Tang. ¹Shanghai Institute of Materia Medica, Chinese Academy of Sciences; ²Shanghai Institute of Materia Medica

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Background Artemisinin and its derivatives were reported to possess strong regulatory effects on inflammation and autoimmune diseases. This study was designed to examine the therapeutic effects and underlying mechanisms of SM934, a water-soluble artemisinin analogue, on lupus-prone mice.

Methods For MRL/lpr mice: *In vivo*, the preventative or therapeutic effects of SM934 in MRL/lpr mice were investigated. *Ex vivo*, the mechanisms of treatment were explored according to the immunologic correlates of disease. Impacts of SM934 on Toll-like receptor (TLR)-triggered B cell responses were evaluated. *In vitro*, the effects of SM934 on the activation and differentiation of CD4 +T cells were examined. For NZB/W F1 mice: *In vivo*, the lupus-prone mice were treated with SM934 for 3 or 6 months respectively to investigate the effect on clinical manifestations and immunological correlates. To further explore the mechanisms of SM934, ovalbumin (OVA)-immunized or interferon (IFN)-elicited C57BL/6 mice were used.

Results *In vivo*, SM934 treatment significantly prolonged the life-span of MRL/lpr mice, ameliorated the lymphadenopathy, decreased the levels of serum anti-nuclear antibodies (ANAs) and the pathogenic cytokines IFN-, IL-6, IL-10 and IL-21, and reduced the proportion of double negative T cells. Treatment with SM934 significantly delayed the progression of glomerulonephritis and improved the survival of NZB/W F1 mice. Clinical improvement was accompanied with decreased anti-dsDNA Abs and serum interleukin IL-17. In addition, SM934 treatment promoted the IL-10 production from macrophages of NZB/W F1 mice, OVA-immunized C57BL/6 mice and IFN-elicited C57BL/6 mice. *Ex vivo*, SM934 treatment elevated the percentage of Treg cells, inhibited the development of Th1 and Th17 cells. Moreover, SM934 suppressed the TLR-triggered activation and proliferation of B cells. *In vitro*, SM934 inhibited the differentiation of Th1 and Th17 cells as well as TLR-associated B-cell activation and plasma cell differentiation. SM934 enhanced IL-10 production from primary macrophages stimulated with IFN-.

Conclusions Taken together, these results demonstrated that the artemisinin analogue SM934 exerted significant therapeutic benefits in lupus-prone mice, by inhibiting both the pathogenic helper T cell development and responses, enhancing anti-inflammatory cytokine IL-10 production and suppressing plasma cell formation. These properties of SM934 might contributed to the restoration of the immune homeostasis in lupus-susceptible mice, and thus cast a light on a novel strategy for lupus treatment.

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