achieved LLDAS at least once; 59 patients achieved LLDAS for≥50% of observations. Multivariate logistic regression analysis showed that age at disease onset< 30 years (OR=0.05, 95%CI [0.01-0.59], p=0.017), 24-hour urine total protein (UTP) level at recruitment (OR=0.9992, 95%CI [0.9987-0.9998], p=0.007), and C3 level (OR=1.004, 95%CI [1.001-1.008], p=0.024) had independent associations with achieving LLDAS for ≥ 50% of all observations (Table 1). During follow-up, 56 (37.6%) patients experienced disease flare including 14 (9.4%) patients with severe flare. Kaplan-Meier analyses showed significant differences in flare rates according to whether LLDAS was achieved and the percentage follow-up time in LLDAS (Figure 1). Multivariate cox analysis revealed that the percentage time of time in LLDAS was an independent negative determinant of disease flare (HR=0.18, 95% CI [0.07-0.48], p=0.001) (Table 2). There were 16 (15.0%)/107 patients who had damage accrual after one year of follow-up. Multivariate logistic analysis showed a tendency for achieving LLDAS during follow-up being protective for damage accrual (OR=0.27, 95%CI [0.07-1.00], p=0.050).

Conclusion: In this Chinese early disease cohort, LLDAS was an attainable goal in clinical practice. Age at onset, UTP and C3 level at recruitment influenced achievement of LLDAS. LLDAS was negatively associated with disease flare and damage accrual; this needs to be confirmed by future longer follow-up.

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AB0377 COMPUTATIONAL DISCOVERY AND PRECLINICAL VALIDATION OF THERAPEUTIC LEADS WITH NOVEL MOAS FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Lupus is a heterogeneous, systemic disease that affects millions of patients globally with a high unmet medical need. We present results from our powerful and efficient computational drug discovery platform that identifies hits with first-in-class mechanisms of action that can advance rapidly and successfully through preclinical validation studies. The twoXAR discovery platform uses an artificial-intelligence framework to integrate diverse patient-derived biomedical data sets to build holistic and unbiased models of human disease biology. The utilization of diverse, proprietary algorithms and deep learning principles provides a highly sensitive platform to elucidate complex disease-specific associations between biology and biomedical data that are integrated with a library of existing drug molecules. This enables the identification of novel, high-value drug discovery hits with known pharmacological properties. The twoXAR platform also preserves interpretable data-driven links to disease biology to facilitate efficient validation and optimization studies.

Objectives: Apply twoXAR's computational drug discovery platform for the discovery of first-in-class lupus therapy hits and perform preclinical characterization of selected hits to identify drug discovery lead molecules.

Methods: Using clinical SLE patient data, we employed the twoXAR platform to build an *in-silico* SLE disease model. Nine molecules with novel mechanisms of action (not previously tested as candidate clinical therapies for lupus) were identified as drug discovery hits and then characterized in preclinical efficacy studies using the MRL mouse model of lupus.

Results: In preclinical validation studies with the MRL mouse model, 2 compounds were differentiated by significant efficacy and excellent tolerability. TXR-711 and TXR-712 increased renal function, decreased renal inflammation and decreased inflammation compared to vehicle-treated control mice. In particular, TXR-711 and TXR-712 significantly decreased serum blood urea nitrogen (BUN) levels, decreased proteinuria levels, and significantly improved kidney histology readouts such as glomerulonephritis and tubule basophilia. Additionally, TXR-711 and TXR-712 treatment resulted in significantly decreased inguinal lymph node weight.

Conclusion: TXR-711 and TXR-712 were identified as SLE drug discovery leads with novel MOAs for further preclinical development. Ongoing studies with TXR-711 and TXR-712 includes pharmacokinetic, pharmacodynamic, and additional MRL mouse efficacy characterization.

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AB0378 UPGRADING THERAPY STRATEGY IMPROVES PREGNANCY OUTCOME IN ANTIPHOSPHOLIPID SYNDROME: A COHORT MANAGEMENT STUDY

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Background: While it is generally agreed that pregnant APS patients should receive personalized treatment, evidence-based guidelines for these patients continue to be lacking.

Objectives: The current study was designed as a management cohort study aiming to evaluate the efficacy and safety of different treatment strategies for pregnant APS patients in the attempt to provide some practical suggestions for attending physicians.

Methods: One-hundred-twenty-seven consecutive pregnancies were assessed; 87 (68.5%) with a history of pregnancy morbidity alone were treated with prophylactic low molecular weight heparin (LMWH)+low-dose aspirin (LDA, 100 mg) [Group I] and 40 (31.5%) with a history of thrombosis and/or severe pregnancy complications with therapeutic LMWH+LDA [Group II]. LMWH doses were increased throughout the pregnancies depending on the patients' weight gain, and treatment was switched to a more intensive one at the first sign of maternal/fetal complications. The study's primary outcome was live births.

Results: There were no significant differences in live birth rate between Group I (95.4%) and Group II (87.5%). Even, fetal complication rate was similar in the two groups; the Group II nevertheless had a higher prevalence of maternal and neonatal complications (p=0.0005 and p=0.01, respectively) and registered a significantly lower gestational age at delivery and birth weight (p=0.0001 and p=0.0005, respectively). Two patients in Group I switched to Group II therapy, six patients in Group II switched to a more intensive treatment strategy (weekly plasma exchange+ fortnightly intravenous immunoglobulins in addition to therapeutic LMWH+LDA). Comparison of the clinical and laboratory characteristics between patients who had shifted to a more intensive therapy and those who did not showed a significant prevalence of history of thrombosis ± pregnancy morbidity (p=0.02, OR 5.96, 95% CI 1.33-26.62) previous pregnancy complications (p=0.02, OR 8.32, 95% CI 1.67-41.3), triple aPL positivity (p <0.0001, OR 97.13, 95% CI 10.6-890) and pregnancy complications (p<0.0001, OR 197,7, 95% CI 10.57-3699) in upgrading group, instead single aPL positivity significantly prevailed (p=0.003, OR 0.06, 95% CI 0.008-0.58) in non-upgrading group. Logistic regression analysis demonstrated that triple aPL positivity was an independent factor for switching to a more effective therapy protocol (p <0.0001, OR 98, 95% CI 10.7-897.54). All eight switched patients achieved a live birth.

Conclusion: Using adjusted LMWH doses and upgrading therapy at the first signs of pregnancy complications led to a high rate of live births in a relatively large group of APS patients. The study outlines the criteria for prescribing appropriate therapy for various subsets of these patients and for switching/upgrading the treatment protocol when it is no longer sufficient. Unfortunately, for the moment there are no evidence-based guidelines on the ideal additional treatment in refractory to conventional therapy APS patients. The present results will hopefully help point the direction of future clinical trials investigating the efficacy and safety of the different therapies on large numbers of APS pregnant patients in order to identify the benefits and limits of different treatment strategies administered from the beginning of pregnancy.

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