patients and controls. Factors associated with sero-reversion of the anti-HPV antibodies were studied by statistical analyses.

Results: 50 SLE patients (age 25.8±3.9 years) and 50 controls (25.8±3.9 years) were vaccinated with Gardasil in 2011. The sero-conversion rates of anti-HPV serotypes 6,11,16 and 18 in patients and controls were 82%, 89%, 95%, 76%, and 98%, 98%, 98%, 80%, respectively, at month 12 post-vaccination. Among those subjects who seroconverted and were available for follow-up, persistence of the antibodies to HPV serotypes 6,11,16 and 18 at 5 years was present in 24/27 (89%), 26/31 (84%), 32/34 (94%), 24/25 (96%) of the SLE patients and 32/32 (97%), 32/32 (97%), 32/32 (100%) and 23/24 (96%) of the controls, respectively. Moreover, antibody titers to HPV serotypes 6 and 16 at 5 years were significantly lower in SLE patients than controls. Seven (21%) SLE patients had sero-reversion of any one of the four anti-HPV antibodies (6,11,16 or 18) at year 5 post-vaccination. Patients who sero-reverted had received a significantly higher cumulative dose of prednisolone (3.14±1.21 vs 1.89±1.28; p=0.03). Among 64 flares in patients with persistent immunogenicity. These sero-reverted patients had also received a non-significantly higher cumulative dose of cyclophosphamide (1.97±5.22 vs 0.43±2.24 grams; p=0.27). In addition, sero-reverted patients had more SLE flares in the 5 years post-vaccination. Antibody titers to HPV serotypes 6 and 16 were significantly lower in SLE patients than controls. Patients with higher anti-HPV antibodies and 26 flares in those with sero-reversion, renal flares occurred more frequently in the latter group of patients (16% vs 38%; p=0.02).

Conclusions: Immunogenicity of the quadrivalent HPV vaccine was retained in SLE patients at 5 year post-vaccination. Antibody titers to HPV serotypes 6 and 16 were significantly lower in SLE patients than controls. Patients with more SLE flares, especially renal flares, and had received higher cumulative doses of glucocorticoids, mycophenolate mofetil and tacrolimus were more likely to have sero-reversion of one or more anti-HPV antibodies. Re-vaccination of these patients should be considered.

Disclosure of Interest: None declared


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MOLECULAR PROFILES ASSOCIATE WITH CLINICAL DISEASE ACTIVITY AND INFORM PATIENT SUBSETTING IN ADULT SYSTEMIC LUPUS ERYTHEMATOSUS


Background: Systemic lupus erythematosus (SLE) is characterised by remarkable clinical and pathophysiological diversity, hindering diagnosis, treatment and treatment development. Subsetting of patients based upon clinical presentations alone has not identified homogeneous groups of patients best treated with a directed therapeutic.

Objectives: To cluster SLE patients into more homogeneous subsets with common molecular pathway signatures, and to assess the clinical, therapeutic, and demographic features enriched in each cluster.

Methods: Serial or single plasma, serum and RNA samples (n=290) were collected from 198 SLE patients who met ACR classification. Disease activity was assessed by modified SELENA-SLEDAI at an average of 17 visits per patient. Transcriptomic co-expression signature module scores were calculated from Illumina Beadchip Microarray gene expression data for 29 immune pathway related modules. Plasma soluble mediators (n=23) and 12 antinuclear autoantibodies (anti-dsDNA, chromatin, ribosomal P, Sm, Sm, SmRNP, RNP, Ro/SSA, La/SSB, centromere B, Scl-70 and Jo-1) were assessed by multiplex bead-based assay and ELISA. Spearman correlations were used for univariate and multivariate analysis using R.

Patients were clustered on module signature scores and soluble mediators using random forest and ISNE.

Results: SLEDAI scores strongly correlated with interferon modules and were modestly correlated with plasmablast and select cell cycle signatures in this adult lupus collection. SLEDAI scores also correlated with soluble levels of IFAna, IL21, IL1a, IL1b, IL10 and MIG. Random forest defined seven clusters of SLE patients with unique molecular phenotypes based upon gene co-expression module signatures and soluble mediators. Infarmeration and interferon (IFN) signatures were elevated in Clusters 1 (moderately) and 4, with decreased T cell signatures in Cluster 4. The other clusters had lower IFN and inflammation signatures, but differed in their monocyte, plasmablast and T cell signatures. Clusters 1 and 4 had the highest SLEDAI scores, with high rates of anti-dsDNA, low complement, proteinuria and hematuria; these features were also prominent in Cluster 3, which lacked the IFN and inflammation signatures. Cluster 6 had the highest plasma-blast module score, highest IL1a levels, and SLEDAI scored rashes, but only moderate IFN and inflammation module scores. Cluster 2 had higher rates of SLEDAI scored alopecia, a slightly elevated inflammation signature, but lower interferon signature and lower soluble mediator levels.

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