Methods Retrospective analysis of new thrombotic events among primary-APS (pAPS) patients followed for up to 15 years in three medical centres in Israel.
Results Among 312 primary-APS patients 143 (46%) had new thrombotic event classified to three patterns: (1) Arterial - associated with heart valve disease (OR 7.24, 95% C.I. 2.26–24.6), hypertension (OR 3, 95% C.I. 1.44–6.25), elevated anti B2-GPI IgM (OR 1.04, 95% C.I. 0.996–1.08), arterial thrombosis at presentation (OR 1.74 CI95% 0.992–3.26) and older age (41 vs. 34 years, p<0.001). (2) Venous – linked with venous thrombosis at presentation (OR 12.9, 95% C.I. 5.27–31.6, p<0.001), heart valve disease (OR 9.81 CI95% 1.82–52.9, p=0.018), aGAPSS (OR 1.15 CI95% 1.02–1.29) and younger age (31 vs. 36.5 years, p=0.001); (3) Combined pattern - associated with heart valve disease (OR 40.5 95% C.I. 7.7- 212) and pulmonary embolism (OR 7.47 95% C.I. 1.96–28.5).

A 4th variant 'the Breakthrough pattern' defined by re-thrombosis despite prophylactic therapy was observed in 100/143(70%) patients and linked with heart valve disease (OR 8. 95% C.I. 2.43–26.3), venous thrombosis at presentation (OR 2.61 95% C.I. 1.47–4.66), leg ulcers (OR 12.2, 95% C.I. 1.4–107), hypertension (OR 1.99, 95% C.I. 0.92–4.34) and higher aGAPSS (OR 1.08, 95% C.I. 0.99–1.18).
Conclusion In this real life observation, re-thrombosis was common among pAPS patients including in those recommended to receive prophylactic therapy. Different patterns of recurrence were identified and linked with presenting symptoms, specific serological markers, APS-manifestations and comorbidities. Studies that will address interventions to prevent recurrences of APS related events are needed.

S03.3 PATIENT-SPECIFIC AND DISEASE-RELATED DETERMINANTS FOR CARDIOVASCULAR DISEASE (CVD) RISK STRATIFICATION IN THE APPLE (ATHEROSCLEROSIS PREVENTION IN PAEDIATRIC LUPUS ERYTHEMATOSUS) CLINICAL TRIAL COHORT

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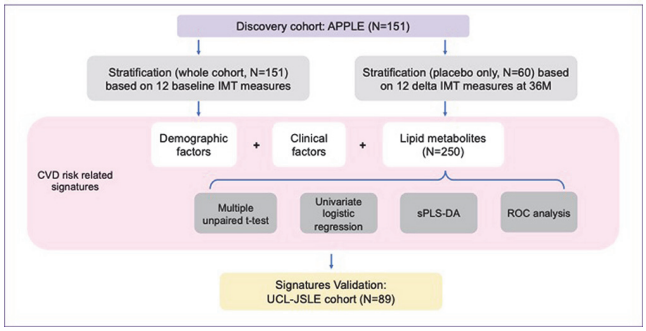
Purpose The risk of developing CVD through atherosclerosis in juvenile-onset systemic lupus erythematosus (JSLE) patients is significantly increased. This study aimed to stratify and characterize JSLE patients at elevated CVD risk using patient/disease-related factors and metabolomic data from patients recruited to the APPLE (Atherosclerosis Prevention in Paediatric Lupus Erythematosus) clinical trial, designed to assess atherosclerosis development.
Methods Unsupervised hierarchical clustering was performed to stratify patients by arterial intima-media thickness (IMT) measurements at baseline (N=151) and carotid (c)IMT progression over 36 months (placebo arm only, N=60). Baseline metabolomic profiles (~250 serum metabolites) were compared between clusters using conventional statistics, univariate logistic regression, sparse Partial Least-Squares Discriminant Analysis (sPLS-DA) and random forest classifier. An independent cohort (UCL-JSLE cohort, N=89) with matching metabolomics, immunophenotyping and proteomics, was used to validate the discovered CVD risk-related signatures from the APPLE cohort.



Abstract S03.3 Figure 1

Results Baseline IMT stratification identified 3 clusters with high, intermediate, and low baseline IMT measurements and progression trajectories over 36 months, each having distinct racial/BMI/household education/income characteristics. Analysis of cIMT progression over 36 months identified 2 patient groups with high and low IMT progression. Unique metabolomic profiles differentiated high and low cIMT progression groups, with good discriminatory ability (0.81 AUC in ROC analysis) using the top 6 metabolites (Total cholesterol esters, Total cholesterol, Phospholipids in small LDL particles, Total cholesterol in small LDL particles, Free cholesterol in medium LDL particles and Total lipids in small LDL particles) selected from the analysis. cIMT progression over 36 months in the placebo group correlated positively with baseline disease activity (SLEDAI), damage score (SLICC), white blood cell count, serum complement C3, blood pressure (both systolic and diastolic) and BMI. Metabolomics signatures discovered from the APPLE cohort were applied to stratify JSLE patients in the validation cohort (UCL-JSLE), where 3 groups were identified with distinct metabolomics profiles indicating JSLE patients with high risk (N= 20), intermediate risk (N= 43) and low risk (N= 26) CVD-risk. Significant differences were observed in the frequency of classical monocytes (p=0.015) and nonclassical monocytes (p=0.005) when comparing high and low CVD risk groups in the UCL-JSLE cohort.
Conclusions Complex analysis of IMT patterns and progression in the APPLE trial cohort identified novel key determinants that could guide further research for CVD-risk stratification in JSLE.

Thursday 06 October 2022 from 17:30 to 19:00

S04 clinical challenges

S04.1 DISEASE ACTIVITY AND CLINICAL REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARISON BETWEEN PATIENT AND PHYSICIAN PERSPECTIVES BY MEANS OF PATIENT REPORTED OUTCOMES (PROS)

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Purpose In daily clinical practice, it is not rare to observe a relevant discordance between patient's global assessment (PGA) and physician's global assessment (PhGA), because of different illness perceptions.

The purpose was to evaluate the presence of PGA/PhGA discrepancy in patients with SLE who were in clinical remission and to evaluate how this discrepancy affects PROs. In addition, to explore whether this discordance could be influenced by the presence of additional elements affecting patients' quality of life, such as sleep disturbances and psycho-emotional factors.

Methods Our study included adult SLE patients consecutively followed in a single Lupus Clinic from March to July 2021 fulfilling at minimum the definition of clinical remission of treatment according to the definition of Zen et al.[1] (cSLEDAI=0, corticosteroids ≤5mg/die, stable dosage of DMARD). Medical records including demographic data, clinical characteristics and outcomes measures were collected. Pain assessment, PGA and PhGA were rated on a visual analogue scale (0–100 mm) on the same day of the clinical evaluation. To analyse the discrepancy between PGA and PhGA, the [PGA-PhGA] variable was calculated, considering as discordant a difference ≥25 mm as previously proposed.[2] All the subjects completed the following questionnaires: Health Assessment Questionnaire (HAQ), SF36 Health Survey, State-Trait Anxiety Inventory (STAI-Y1/Y2), Self-rating Depression Scale (SDS Zung) and Insomnia Severity Index (ISI). Statistical analysis was performed to compare concordant and discordant groups.

Results The study included 106 patients, (93 women, 13 men) with a median age of 48 (41–58) and a median SLE duration 227 months (124–330). At the last evaluation median SLEDAI was 0 (0–2) and median SLICC was 1 (0–1). According to Zen definitions of remission, 51 patients (48%) and 20 (19%) also fulfilled the criteria of clinical remission of corticosteroids and complete remission respectively. Nevertheless, in 24 patients (22,7%) [PGA-PhGA]≥25. Patients in the discordant group were older and less frequently achieved the definition of clinical remission of corticosteroids (see table1) than concordant. No differences were found in gender, SLE duration, serology, disease activity or damage and other treatment. Data about differences in PROs between two groups are reported in the Table 1: discordant patients had a worse performance in all the PROs included in the study. At multivariate analysis SF-36 Physical Component Summary (PCS) resulted associated with [PGA-PhGA]≥25 (p=<0,0001).

Conclusions In our study we found that, even in patients considered in remission, in more than 20% of patients there is a considerable discordance between the global disease assessment reported by patients and their physicians. Patients that had a higher PGA also presented worse score at PROs. Our data seems to confirm that potential causes for discordance could be more related to the presence of non-inflammatory processes, depression, or anxiety than clinical manifestations or damage related to SLE.

REFERENCES

1. Zen *et al. Ann. Rheum. Dis*. 2015;**74**:2117–2122
2. Neville C, *et al. J Rheumatol* 2000;**27**:675–9

Abstract S04.1 Table 1 Data are expressed as absolute number and percentage or median and interquartile range (IQR) and compared using Mann-Whiteney test or Chi Squared test

	TOTAL N=106 (%)	CONCORDANT GROUP (PGA-PhGA) <25 N=82 (%)	DISCORDANT GROUP (PGA-PhGA) ≥25 N=24 (%)	P value
Age at evaluation, years	48 (42-58)	46 (39-57)	58 (49-62)	p=0,0043
Clinical remission of corticosteroids	51 (48,1)	47 (57.3%)	4 (16.7%)	p<0.001; OR 6,7; CI95% 2.1- 21
VAS-pain [0-100],	10 (0-30)	10 (0-20)	50 (40-60)	< 0.001
SF-36 Physical Component Summary (PCS)	50 (37,5-53)	51 (44-54)	30 (27,5-39)	< 0.001
SF-36 Mental Component Summary (PCS)	48 (38-55)	51 (40-55)	40 (36-48,5)	0,015
STAI-Y1 [20-80]	35 (30-47)	33 (28,3-45,5)	42 (36,5-49,5)	0,013
STAI-Y2 [20-80]	37 (30-46)	35 (29-43,3)	42 (36-46)	0,021
Test di Zung [20-80]	34,5 (29-43)	33 (27-43)	39 (35,5-44,5)	0,008
Insomnia severity index [0-28]	6 (2-12)	4 (1-9)	9 (6,8-14,3)	<0,0001
HAQ	0 (0-0,1)	0 (0-0)	0,38 (0-0,6)	< 0.001