Table 1. Vascular events vs. antiphospholipid antibodies (manufacturer's cut-off applied) in the included patients with recent-onset SLE during the study period (*n* = 270).

Vascular event (VE)	All VEs, n (%)	High risk aPL (n=40)	Low risk aPL (168)	aCL IgG ever positive (n=127)	aCL IgM ever positive (n=98)	aB2GP1IgG ever positive (n=42)	aB2GP1IgM ever positive (n=116)	LAC ever positive (n=66)	Triple positive (31)
All VE	20(7.4)	12(60)	8(40)	14(70)	12(60)	9(45)	16(80)	4(20)	3(15)
Any arterial event	7(2.5)	4(57)	3(33)	6(66)	4(44)	4(44)	7(77)	3(33)	2(22)
Stroke	3(1)	1(33)	2(67)	2(66)	1(33)	2(66)	2(66)	0(0)	0(0)
MI	1(0.35)	0(0)	1(100)	1(100)	0(0)	0(0)	1(100)	0(0)	0(0)
Peripheral limb ischemia	2(0.7)	2(100)	0(0)	1(50)	1(50)	1(50)	1(50)	2(100)	1(50)
Any Venous event	15(5.5)	10(67)	5(33)	9(64)	8(57)	6(42)	7(50)	3(21)	2(14)
Pulmonary Embolism	2(0.7)	1(50)	1(50)	2(100)	2(100)	2(100)	1(50)	1(50)	1(50)
Deep Venous Thrombosis	10(3.7)	7(70)	3(30)	5(71)	4(57)	3(42)	6(85)	1(14)	1(14)
Cerebral Venous Thrombosis	3(1)	2(67)	1(33)	2(66)	2(66)	1(33)	2(66)	1(33)	0(0)
Catastrophic APS	1(0.35)	1(100)	0(0)	1(100)	1(100)	0(0)	1(100)	1(100)	1(100)
Pregnancy morbidity	1(0.35)	1(100)	0(0)	0(0)	1(100)	0(0)	1(100)	1(100)	1(100)

positive (Figure 1b-1c). Baseline dual or triple positive tended to have a stable positive aPL profile and persisted to show aPL antibodies on follow-up (Figure 1d-1e). Significant fluctuations were observed in β2GPI IgM and aCLA IgM compared to other aPL antibodies. High-risk aPL profiles were identified in 40 (19.2%) patients, while 168 (80.8%) had low-risk profiles (Figure 1a). Vascular events (VE) occurred in 20 (7.4%) patients at 2-year of follow up, details of the vascular events and aPLs association are in Table 1. There was a significantly higher incidence of VE in high-risk aPL (12/40, 30%) compared to low-risk aPL group (8/168, 4.7%, p<0.001, OR:8.57,95%CI: 2.88-26.16) and similar pattern was seen in the persistently positive (12/52, 23.1%) vs the group with aPL fluctuation (8/130, 6%, p<0.001,OR:4.58,95%CI:1.57-13.76).

Conclusion: Longitudinal assessment of aPL titres reveals significant fluctuations, with a subset of patients transitioning to persistent positivity or negativization. High-risk aPL profiles and persistent positivity are critical predictors of vascular events in SLE.

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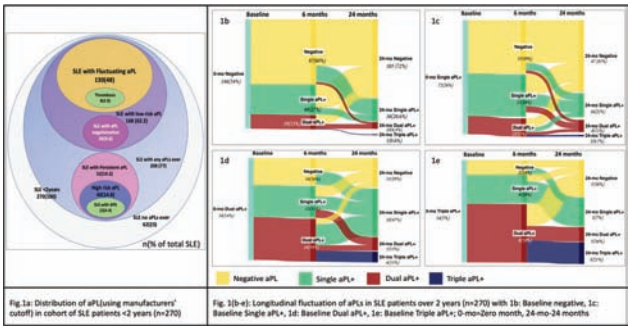

Fig.1a: Distribution of aPL(using manufacturers' cutoff) in cohort of SLE patients <2 years (n=270)

Fig. 1(b-e): Longitudinal fluctuation of aPLs in SLE patients over 2 years (n=270) with 1b: Baseline negative, 1c: Baseline Single aPL+, 1d: Baseline Dual aPL+, 1e: Baseline Triple aPL+; 0-mo=Zero month, 24-mo-24 months

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Basic and Clinical Abstract Sessions: Making pain less painful

OP0275 POTENTIAL DRUG TARGETS FOR CHRONIC WIDESPREAD PAIN: A PROTEOME-WIDE MENDELIAN RANDOMIZATION AND DRUG REPURPOSING ANALYSIS

Keywords: Biomarkers, Artificial Intelligence

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Background: Chronic widespread pain (CWP) is a common and debilitating condition characterized by persistent pain across multiple body regions. Recent advances in protein-profiling techniques enable measurements of blood proteins at scale and research into drug repurposing.

Objectives: This study aimed to identify therapeutic targets associated with CWP.

Methods: We used proteome-wide Mendelian randomization (phenome-wide MR) and colocalization analyses to assess potential causal effects of plasma proteins related to CWP phenotypes. The CWP GWAS data included 435,971 participants (2,149 cases) from the UK Biobank; protein quantitative trait loci (pQTL) data was available for 54,219 participants. Cis-SNPs ($p < 5 \times 10^{-8}$) within 1 Mb of protein-coding genes, with LD clumping ($r^2 < 0.001$) and an F-statistic > 10 were used as instrumental variables for each corresponding protein. For those proteins with marginal significant associations ($p < 0.05$), colocalization analyses were used to test the impact of linkage disequilibrium (H4, a measure of the likelihood that the genetic variant influences both the protein and disease). Finally, we searched potential existing therapies for repurposing based on their action on target proteins.

Results: We identified 101 plasma proteins significantly associated with CWP, of which 8 showed strong evidence of colocalization. Among these, LONP1, CD22, FAP, and KHK were associated with an increased risk of CWP (OR ranging from 1.40 to 2.08 and H4 values > 0.583), while FXYD5, AMPD3, COMMD1, and ADAMTSL2 were associated with a decreased CWP risk (OR between 0.39 and 0.66, H4 values ranging from 0.569 to 0.993). Notably, **CD22** and **FAP** are already targeted by existing drugs, indicating their potential for repurposing: inotuzumab, ozogamicin and moxetumomab pasudotox; and f19 131i and sibrotuzumab respectively.

Conclusion: We identified 8 potential protein targets for CWP, with CD22 and FAP already targeted by existing drugs. These findings provide insights into the molecular mechanisms underlying CWP, and suggest repurposing opportunities for drug development and clinical testing.

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Disclosure of Interests: None declared.

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OP0276 GUT DYSBIOSIS AND VAGUS NERVE: A PATHWAY TO CHRONIC PAIN IN RHEUMATOID ARTHRITIS

Keywords: Microbiome, Animal Models, Pain, Gastrointestinal tract

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Background: Emerging evidence highlights the pivotal role of the vagus nerve (VN) in rheumatoid arthritis (RA), with reduced VN activity preceding the disease onset and vagotomy identified as a potential risk factor for RA development. This phenomenon is linked to the VN's immunomodulatory properties but may also