P41 **ASSESSMENT OF COGNITIVE FUNCTION IN A RANDOMIZED, PLACEBO-CONTROLLED, INTERVENTIONAL TRIAL CONDUCTED IN PATIENTS WITH MODERATE-TO-SEVERE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

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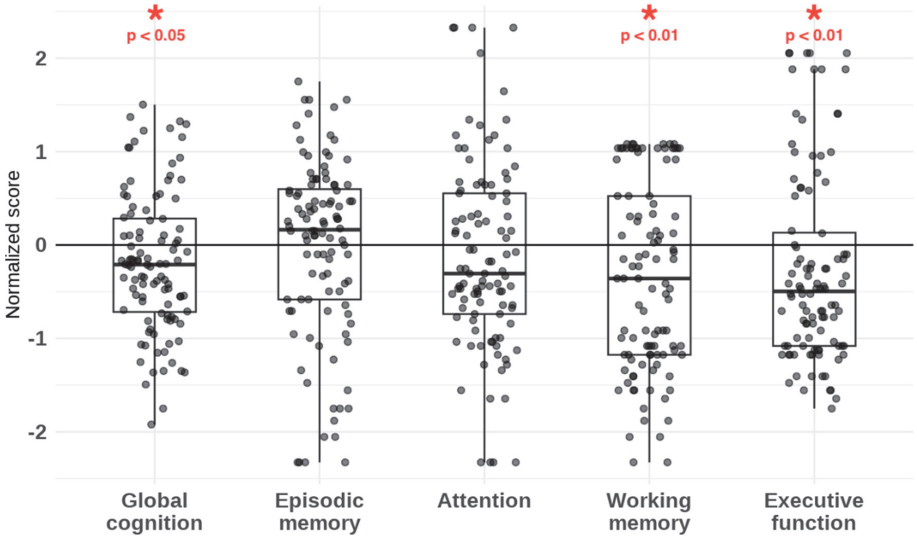
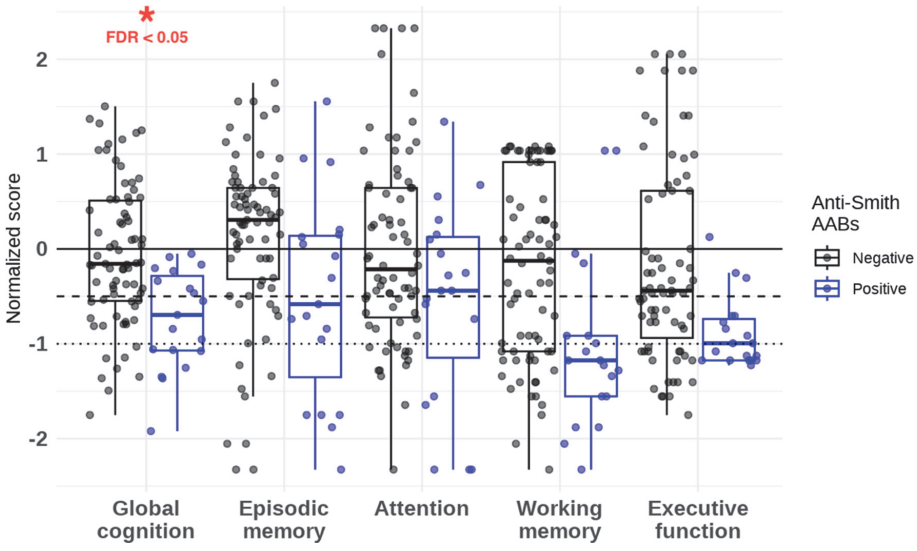
Objective Cognitive dysfunction is a characteristic yet heterogeneous feature of systemic lupus erythematosus (SLE) that can impact quality of life. In a phase 2 trial (NCT03656562) comprising two separate, placebo-controlled cohorts evaluating ianalumab and iscalimab in patients with SLE of moderate-to-severe activity, we employed Cambridge Automated Neuropsychological Test Battery (CANTAB) assessments to characterize patients' baseline cognitive function and explore associations with clinical parameters and biomarkers associated with disease severity. Here we report baseline results, with further exploration of potential treatment effects in the ianalumab cohort.

Methods CANTAB was administered at baseline, 12 and 28 weeks. Scores indexed episodic memory, working memory, executive function and attention, normalized by age and gender relative to individuals without known cognitive dysfunction. A global composite comprised the mean of four domain scores for each assessment.

Results Baseline CANTAB scores (n=104 patients) indicated cognitive dysfunction in this sample for executive function, working memory, and global cognition (t-test for group mean <0; figure 1). Correlations between cognitive assessment scores and standard clinical (e.g., FACIT-Fatigue) and biomarker parameters of disease activity were generally low, with the highest correlation observed between global cognition and anti-Smith antibody status (r= -0.4, FDR <0.05; figure 2). Although the primary lupus disease outcome objective was met for the ianalumab treatment cohort (n=64; reported



Abstract P41 Figure 1 Baseline CANTAB scores across assessed cognitive domains



Abstract P41 Figure 2 Baseline CANTAB scores grouped by anti-Smith antibodies status

separately), we did not observe a treatment effect on CANTAB scores. In consideration of heterogenous cognitive dysfunction in SLE, we explored treatment effect heterogeneity using biomarkers and clinical parameters putatively associated with cognitive dysfunction in SLE. Here, a SomaScan® aptamer to complement component C1q showed a significant treatment interaction for working memory and executive function.

Conclusions These results are consistent with a heterogenous profile of cognitive dysfunction in SLE. However, limited association between CANTAB scores and clinical and laboratory disease markers makes clinical interpretation challenging. We did not detect an ianalumab treatment effect after 28 weeks but cannot exclude the possibility of benefit over longer treatment intervals, or detection by more frequent CANTAB assessments. SLE trials testing treatment effects on cognitive function may benefit from stronger biomarkers to identify individuals experiencing disease-related cognitive dysfunction most likely to benefit from an efficacious therapy.

P42 MANAGEMENT AND CLINICAL OUTCOMES IN 359 PATIENTS WITH SLE FOLLOWED LONG-TERM IN A SPECIALIST CENTRE – EFFECT OF SEX, ETHNICITY AND AGE AT PRESENTATION

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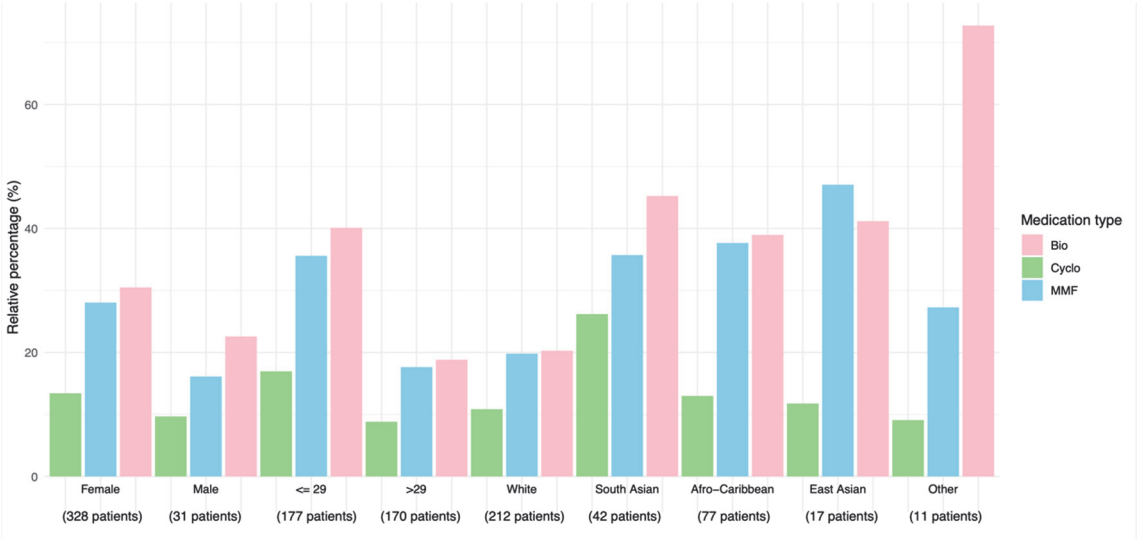
Objective The Lupus Clinic at University College London Hospital (UCLH) has been recruiting patients since 1978.We carried out a comprehensive study of the records of patients from the clinic to study changes in management and outcomes in different groups of patients. In this abstract we investigate differences in management and outcome between patients of different sex, ethnicity and age at presentation.

Methods The study population consists of 359 patients recruited to the cohort between 1978 and 2011 for whom we have comprehensive data regarding start and end of follow-up, demography, ever-use of cyclophosphamide, mycophenolate and/or biologics, presenting features and mortality. The median length of follow-up was 14 years (min 0.5, max 40). In this study we classified them into groups according to sex, ethnicity (White, African/Caribbean, South Asian, East Asian and other) and age at time of presentation to UCLH (classified as either above or below the median, which was 29 years).

Results Overall, 79 patients ever received cyclophosphamide, 98 mycophenolate and 107 biologics. Fifty-two patients died of whom 21 died within 10 years of presentation. Table 1 shows the differences between groups in terms of clinical manifestations at presentation and mortality within 10 years of presentation. African/Caribbean and South Asian patients were significantly more likely to present with features outside skin and joints as were those diagnosed younger. Figure 1

Abstract P42 Table 1 Mortality within 10 years, and severity of presenting manifestations

Category	Mortality within 10 years		p	Presenting features		p
	YES	NO		Mild .i.e. skin/ joint only	Not mild – all other features	
Sex						
Female (n=325)	20	305	0.45	139	186	0.24
Male (n=34)	1	33		11	23	
Ethnicity						
White (n=212)	16	196	0.31	107	105	**0.0014**
African/ Caribbean (n=77)	1	76		21	56	
South Asian (n=42)	3	39		11	31	
East Asian (n =17)	1	16		7	10	
Other (n=11)	0	11		4	7	
Age at presentation						
≤29 years	12	177	0.67	74	115	**0.012**
>29 years	9	161		76	94	



Abstract P42 Figure 1 Use of cyclophosphamide, mycophenolate and biologics in different groups