A MULTIANALYTE ASSAY PANEL WITH CELL-BOUND COMPLEMENT ACTIVATION PRODUCTS DEMONSTRATES CLINICAL UTILITY IN SYSTEMIC LUPUS ERYTHEMATOSUS

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SUPPLEMENTARY MATERIAL

Exclusion criteria

Exclusion criteria were previous diagnosis of SLE by the investigator; treatment with immunosuppressants or corticosteroids > 5 mg/day prednisone or equivalent in the month before blood draw for the MAP; active cancer, pregnancy, lactation, or HIV infection at the time of blood draw. Active infection with fever within 2 days of blood draw was also an exclusion criterion. Upon review of the exclusion criteria of the patients in the list, the investigators notified Exagen's team so that patients who met one or more exclusion criteria could be replaced with others within the same MAP score group (negative; low tier-2; high tier-2; tier-1).

Number of charts reviews and time of visits

Apart from one site that reviewed charts of 11 patients, all practices reviewed charts as multiples of 5 (two negative, one low tier-2, one high tier-2, and one tier-1) from a minimum of 5 to a maximum of 25 patients per site (n=5, 10, 15, 20, and 25 patients from 4, 1, 2, 2, and 2 practices, respectively). Charts of patients who met exclusion criteria (n=201) were not reviewed (Figure 1).

T1 occurred for all 161 subjects an average of 41 days after T0 (median 23 days, interquartile range [IQR] 14 – 42). T2 was defined as the last patient visit and could be included in the study as long as it took place at least 8 months after T1. T2 was performed for all patients whose charts were available for review and no attempts were made to maintain the proportion of 2:1:1:1 among the 4 MAP score groups. Ten of the 12 sites performed 90 (56%) chart reviews (35 negative, 19 low tier-2, 13 high tier-2, 23 tier-1) at T2 (Figure 1). T2 occurred on average 444 days after T0 (median 364 days, interquartile range [IQR] 318 – 495).

1982/1997 ACR classification criteria (1)

At T0, ANA positivity was indicated as an ACR criterion for 124 (77%) of patients. A small number of patients (n=21, 13%) fulfilled the ACR classification criteria of SLE at this visit. Consistent with other patient populations suspected of SLE, the most common clinical classification criteria at T0 were arthritis (n=75, 47%) (2,3), photosensitivity (n=40, 25%) and malar rash (n=32, 20%) (4,5). In this patient population, the hematological criterion was indicated only in 19 patients (12%), possibly because of lower availability or less extensive review of lab results compared to other populations (2).

Hazard of assigning ICD-10 sections other than M32

The hazard of assigning the ICD-10 section for other systemic involvement of connective tissue (M35, newly indicated in 18 patients since T0) was lower in the tier-1 group than in the negative, as no tier-1 positive were assigned M35 (no events). Using the MAP negative patients as reference, the hazard of

assigning the ICD-10 section M35 was 6.4-fold higher in the low tier-2 (hazard ratio = 6.4, 95% CI, 1.3-30.8, p=0.021), 12.7-fold higher in the high tier-2 (hazard ratio = 12.7, 95% CI, 2.6-62.1, p=0.002), and was lower for the tier-1 (hazard ratio = 0 because of no events).

There were no significant associations between the MAP score group and the hazard of assigning the ICD-10 section of fibromyalgia (M79.7, newly indicated in 11 patients since T0, p=0.1), rheumatoid arthritis (M05, newly indicated 6 patients since T0, p=0.09), or other commonly indicated ICD-10 section, such as vitamin D deficiency (E55, newly indicated in 14 patients since T0, p=0.4), joint disorder (M25, newly indicated in 6 patients since T0, p=0.8), or unspecified osteoarthritis (M19, newly indicated in 13 patients since T0, p=0.2) (data not shown).

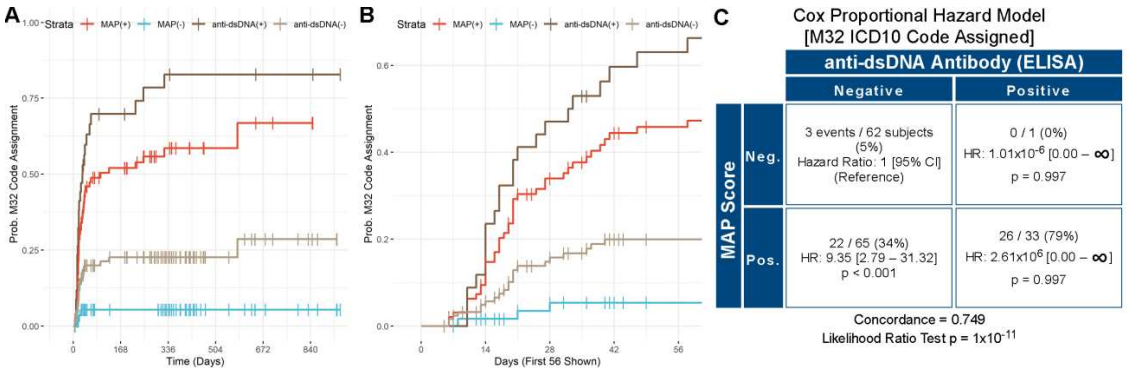
Supplementary Table 1. Race/ethnicity distribution in the 4 patient groups.

	Negative	**Low tier-2**	**High tier-2**	**Tier-1**
White	47 (74.6%)	27 (81.8%)	20 (62.5%)	20 (60.6%)
Black	11 (17.5%)	3 (9.1%)	8 (25%)	12 (36.4%)
Asian	2 (3.2%)	1 (3%)	0 (0%)	0 (0%)
Hispanic	1 (1.6%)	0 (0%)	2 (6.2%)	1 (3%)
Native Americans	1 (1.6%)	0 (0%)	0 (0%)	0 (0%)
Others	1 (1.6%)	2 (6.1%)	2 (6.2%)	0 (0%)
Total	63 (100%)	33 (100%)	32 (100%)	33 (100%)

Values represent the number and percentage (%) in each category.

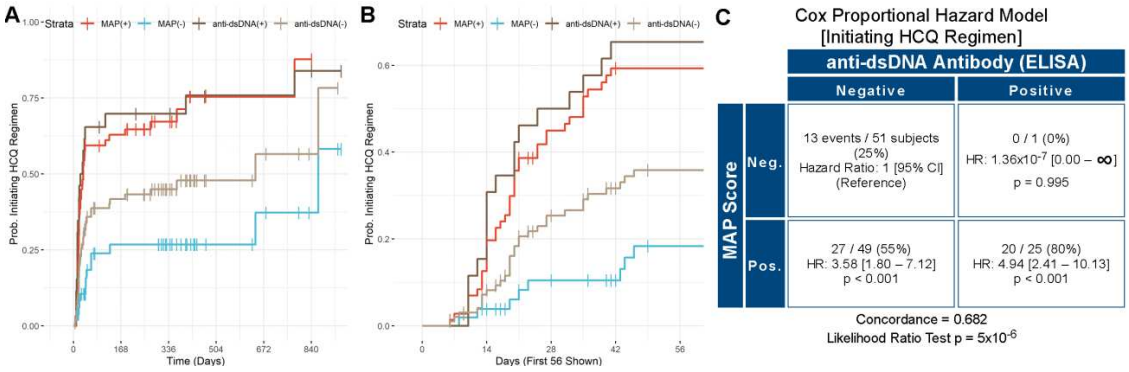
Supplementary Figure 1. Survival analysis (M32)

Panels A and B. Kaplan-Meier time-to-event curves for assignment of the M32 ICD-10 section over time. Curves show the percent probability of assignment of the M32 section after T0 for MAP positive (MAP(+)), MAP negative (MAP(-)), anti-dsDNA positive (anti-dsDNA(+)), and anti-dsDNA negative (anti-dsDNA(-)) patients throughout the study. The X-axis reports the number of days since T0. Panels A and B report the same data analysis, with panel B allowing better visualization of the initial portion of the survival curves. **Panel C**. Cox proportional hazard model comparing the MAP score (Neg.: negative; Pos.: positive) vs. anti-dsDNA antibodies for assignment of the M32 section. In each quadrant, the numerators represent the number of subjects that were assigned an M32 section after T0 (events, n=51 in total) while the denominators represent all subjects in that quadrant. Concordance and p value of the likelihood ratio test are also reported. For data analysis, we used the date of the visit when the M32 section was recorded in the ICD-10 list.



Supplementary Figure 2. Survival analysis (HCQ)

Panel A and B. Kaplan-Meier time-to-event curves for use of HCQ over time. Curves show the percent probability of using HCQ after T0 for MAP positive (MAP(+)), MAP negative (MAP(-)), anti-dsDNA positive (anti-dsDNA(+)), and anti-dsDNA negative (anti-dsDNA(-)) patients throughout the study. The X-axis reports the number of days since T0. Panels A and B report the same data analysis, with panel B allowing better visualization of the initial portion of the survival curves. **Panel C**. Cox proportional hazard model comparing the MAP score (Neg.: negative; Pos.: positive) vs. anti-dsDNA antibodies for use of HCQ. In each quadrant, the numerators represent the number of subjects on HCQ after T0 (events, n=60 in total) while the denominators represent all subjects in that quadrant. Concordance and p value of the likelihood ratio test are also reported. For data analysis, we used the date of the visit when HCQ use was recorded in the medication list.



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