51/1000 py, 26% of SIs were pneumonia and 1% were opportunistic infections. The HR for SI was 5.4 (95% CI: 4.8 to 6.2) comparing SLE to non-SLE. Six percent of the SLE group experienced more than one SI over the study period. The rate of SI allowing for multiple events was 92/1000 py which varied over time since diagnosis (figure 1).

**Conclusions** The rate of SI in SLE is five times the rate in the general population, and remains high in the years following SLE diagnosis. The role of SLE treatments in infection risk should be investigated.

## S6a – Mantenaince Therapy

### S6A:4 A POPULATION-BASED STUDY ON MORTALITY AND THE INFLUENCE OF MEDICATION USE IN 4356 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND 21845 MATCHED CONTROLS FROM THE UNITED KINGDOM

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10.1136/lupus-2018-abstract.33

**Purpose** To estimate the magnitude of the risk from all-cause, age-specific, sex-specific, and cause-specific mortality in patients with SLE and relative risks compared with matched controls, and to evaluate the influence of medication exposure on mortality risk in SLE.

**Methods** We conducted a population-based cohort study using the Clinical Practice Research Datalink, Hospital Episode Statistics, and national death certificates (from 1987 to 2012). Each SLE patient (n=4356) was matched with up to 6 controls (n=21845) by age and sex. Multivariate Cox regression analysis estimated adjusted relative rates (RR) of mortality, and time interaction terms to evaluate mortality timing patterns. Time-dependent Cox models were used to evaluate the association of glucocorticoid use and hydroxychloroquine use on mortality and were adjusted for age, sex, lifestyle parameters, comorbidities and comedication.

**Results** A total of 442 out of 4356 SLE patients died during the study period. Patients with SLE had an increased mortality rate for all-cause mortality compared with age- and sex-matched subjects, after adjustment for confounders (adjusted RR 1.80, 95% CI: 1.57 to 2.08). The RR was highest in patients aged 18–39 years (adjusted RR 4.87, 95% CI: 1.93 to 12.3). Moratlity rates were not defferent between male and female patients. Glucocorticoid use in the previous six months raised the mortality rate while the adjusted RR was 45% decreased with low dose hydroxychloroquine use. SLE patients had increased cause-specific mortality rates for cardiovascular disease, infectious disease, noninfectious respiratory disease and for death due to accidents or suicide, while mortality rate for cancer was reduced, compared to age- and sex-matched subjects.The mortality rate was significantly increased for patients with a history of dementia, seizures, diabetes, cancer, and renal disease (table 1).

**Conclusions** Patients with SLE have a 1.8-fold increased mortality rate compared with the general population. Gluococorticoid use, female sex and young age are associated with an increased mortality risk while low dose hydroxychloroquine use significantly reduces the mortality rate. In addition, special attention should be paid to lupus patients with neuropsychiatric complications, diabetes, malignancy or renal disease since these subgroups of patients are at high risk of death.

### S6A:5 THE 3RS STRATEGY ONE YEAR LATER: STILL REACHING THE GOAL

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10.1136/lupus-2018-abstract.34

**Abstract S6A:4 Table 1** Risk of all-cause monthly within SLE patients (n=4356), stratified according to organ damage (reference = no risk factor)

| | Person years (x1000) | Deaths | IR (/1000) | Adjusted RR* (95% CI) |
|---|---|---|---|---|
| **Dementia** | **0.1** | **14** | **140.0** | **2.99 (1.74-5.14)** |
| **Seizures** | **1.4** | **37** | **26.4** | **2.33 (1.66-3.28)** |
| **Cerebrovascular event** | 1.9 | 73 | 38.4 | 1.28 (0.99-1.65) |
| **Renal disease** | **2.0** | **86** | **43.0** | **1.40 (1.09-1.78)** |
| **Osteoporotic fracture** | 5.1 | 110 | 21.6 | 1.06 (0.85-1.32) |
| **Use of antidiabetics** | **0.9** | **45** | **50.0** | **1.90 (1.39-2.59)** |
| **Malignancy** | **2.0** | **95** | **47.5** | **1.90 (1.50-2.40)** |

* Adjusted for: recent use of corticosteroids, recent use of antimalarials, and recent use of benzodiazepines

**Purpose** Long term immunosuppressive therapy (IST) in systemic lupus erythematosus (SLE) requires constant adjustment according to severity and organ involvement. This ongoing study aims to implement hydroxychloroquine therapy, reduce unnecessary IST, while achieving disease remission without worsening damage.
**Methods** A 3Rs strategy (Reduction, Replacement and Refinement) was implemented and therapy adjusted considering overall disease activity and safety profile. SLE patients from a single centre were followed between January 2013 and July 2017. Inclusion criteria: ACR criteria fulfilment; diagnosis from >1 year. Demographic and clinical features were registered at inclusion; SLEDAI-2K, therapy and flares recorded at inclusion and at each visit. SLICC damage index was calculated at inclusion and at the end. Data were analysed using SPSS.
**Results** At inclusion (n=79), 94% were females, median age 45 (IQR 36–57), mostly Caucasians (89%). Median disease duration was 13 (IQR 7–20). SLEDAI-2K at inclusion was <3 (inactive disease) in 63 (80%). Patients with active disease (SLEDAI-2K>3) at baseline were younger, with less disease duration, not enriched for a specific phenotype. Percentages of azathioprine and mycophenolate were reduced from 35 and 8 to 23 and 6, respectively, similar to interim results (39 months); hydroxychloroquine use remained >70% (10 discontinuations due to retinopathy). In contrast, steroids were steadily reduced from 68% to 42% and are now used at <6 mg/day in 22/33 patients. Importantly, steroid reduction or withdrawal rate was significantly higher in inactive disease group. Belimumab was maintained in 8 patients. Flare occurrence was higher in active disease patients (73% vs 17%, overall 27%). Most episodes were mild. Patients with flares were younger, with higher SLEDAI-2K and steroid dose at inclusion. No treatment discontinuation was associated with flare, except for azathioprine, mostly stopped due to safety profile. During the study, median SLICC damage index augmented from 0 to 1, frequently in the ophthalmological domain. Three patients died and ten were lost to follow-up from 39 to 54 months.
**Conclusions** The 3Rs strategy allowed to reduce unnecessary IST, especially in low disease activity group. Flares rates were in accordance to recent reports. In a long term perspective, our quest to reduce steroid burden seems promising.

## S6A:6 SCREENING IN PATIENTS AT HIGH RISK OF HYDROXYCHLOROQUINE RETINAL TOXICITY

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10.1136/lupus-2018-abstract.35

**Background/purpose** Despite effectiveness and favourable safety profile, antimalarials have the potential to cause irreversible macular retinopathy. Screening methods have evolved over the last decade and the optimal dose of hydroxychloroquine (HCQ) is now set at under 5 mg/kg real body weight. HCQ in Portugal comes only as a 400 mg pill and in 10 pills per package, which is neither friendly for optimising safe dosing nor for promoting compliance. This study aims to test the frequency of retinal hydroxychloroquine toxicity in a single-centre cohort.
**Methods** Cross-sectional study conducted between January-2016 and May-2017, of a convenience sample of chronically compliant and well characterised patients. The screening strategy consisted of automated threshold visual fields and objective test: spectral-domain optical coherence tomography, fundus autofluorescence and multifocal electroretinogram. Toxicity was diagnosed on the basis of compatible visual fields defects together with at least one positive objective test. Univariate statistical analysis was performed using the Wilcoxon Mann-Whitney (WMW) and Chi-Square (CS) tests for non-parametric distributed data.
**Results** Of the 62 patients screened, 32 (51%) had no prior ophthalmological examination. Median age was 46 years (y), IQR 37–60; range 27–83; 59 (95%) were female; the majority, 28 (45%) took HCQ due to SLE, 4 (6%) for Sjögren syndrome, 12 (19%) for UCTD, 11 (18%) for incomplete/cutaneous forms of lupus and 7 (11%) for other CTD. No patient had concomitant renal or liver disease. Median duration and cumulative dose were respectively 8 y (IQR 3–12; range 0.4–31) and 1168 g (IQR 584–2044; range 36–8760). Retinal toxicity was confirmed in 6 SLE and 1 non-SLE patient; in all HCQ was stopped (2/7 screen-naïve; 1/7 on tamoxifen; 1/7 with visual loss). Toxicity correlated to disease (p=0,003) and HCQ therapy (p=0,002) duration, cumulative HCQ dose (p=0,001) and SLE (p=0,04). Table 1 dose adjustments were performed in 13 patients.
**Conclusion** Using a standardised referral protocol for HCQ retinopathy screening led to cessation of therapy due to toxicity (11%) and adjustment of daily dosing (21%). This study highlights that regular adjustment of dose and retinal toxicity screening is mandatory in patients on prolonged HCQ therapy and reinforces lobbying for more flexible dosages. In addition, HCQ toxicity raises the need for alternative therapies in patients with CTD.

**Abstract S6A:6 Table 1** Univariate analysis comparing patients according to retinal toxicity

| Characteristic | Retinal toxicity (n=7) | No Retinal toxicity (n=55) | P value (*sig) | Statistical test |
|---|---|---|---|---|
| Age y (mean±SD) | 50±11 | 49±16 | 0,764 | WMW |
| Non-Caucasian (n, %) | 1 (14) | 7 (13) | 1.000 | CS |
| Disease duration y (mean±SD) | 21±9 | 10±7 | 0,003* | WMW |
| Duration HCQ therapy y (mean±SD) | 17±7 | 8±6 | 0,002* | WMW |
| Current HCQ > 5 mg/kg (n,%) | 6 (86) | 38 (69) | 0,06 | CS |
| Cumulative HCQ g (mean±SD) | 2976±1381 | 1253±1339 | 0,001* | WMW |
| SLE (n,%) | 6 (86) | 22 (40) | 0,04* | CS |

## S6A:7 EXPLORER STUDY: RITUXIMAB USE IN SYSTEMIC LUPUS ERYTHEMATOSUS, A NEW LOOK ON OLD DATA

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10.1136/lupus-2018-abstract.36

**Background** Even if randomised trials EXPLORER and LUNAR failed to prove the superiority of rituximab versus