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DELAY IN DIAGNOSIS REDUCES OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS – CROSS SECTIONAL ANALYSIS OF A GERMAN LONG-TERM STUDY (LULA COHORT)

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Purpose Our aim was to study the delay from the onset of symptoms to the diagnosis of systemic lupus erythematosus (SLE) and its association to the outcome of the disease.

Methods Information on demographics, onset of first symptoms, first physicians visit and time of diagnosis was assessed by self-reported questionnaires among SLE patients in Germany in 2010 (LuLa cohort, n=585). Disease activity (Systemic Lupus Activity Questionnaire; SLAQ), disease related damage (Brief Index of Lupus Damage; BILD) and health related quality of life were chosen as relevant proxies for outcome. Linear regression analysis was used to analyze the association to the outcome of the disease, adjusted for age, disease duration and sex.

Results Mean reported duration between the onset of symptoms and the diagnosis of SLE was 45.7 months (SD 72.6), including a mean duration of 13.2 month (SD 40.9) between the onset of symptoms and the first physicians visit. In our cohort, the mean disease duration was 17.7 years (SD 7.89). A delayed diagnosis was associated with high disease activity (SLAQ, $p < 0.0001$, $\beta = 0.199$, corr. $R^2 = 0.068$), high disease-related damage (BILD, $p = 0.002$, $\beta = 0.137$, corr. $R^2 = 0.163$) and low health-related quality of life (SF-12 physical $p = 0.004$, $\beta = -0.136$, corr. $R^2 = 0.125$, SF-12 mental $p = 0.004$, $\beta = -0.143$, corr. $R^2 = 0.012$) in the year 2010. The organ involvement at the time of diagnosis did not alter these results.

Conclusion The time to diagnosis was associated with a worse outcome in systemic lupus erythematosus, assessed by self-reported questionnaires for disease activity, disease-related damage and quality of life, unaffected by the organ involvement at the time of diagnosis. An early diagnosis should therefore be strived to improve the long-term outcome of the disease.

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PREDICTORS OF TREATMENT OUTCOME IN PATIENTS WITH PROLIFERATIVE LUPUS NEPHRITIS: A 36-MONTH RETROSPECTIVE COHORT STUDY

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Background The EULAR/ERA-EDTA recommendations for lupus nephritis state that renal response should be achieved in 12 months following induction therapy. However, early predictors of renal outcome are not well established. We aim to identify baseline predictors of complete renal response (CRR).

Methods Retrospective cohort study over 36 months including patients with SLE fulfilling the ACR'97 and/or the SLICC'12

classification criteria and with a biopsy-proven proliferative lupus nephritis (class III/IV), enrolled in the CHUC Lupus Cohort. CCR was defined according to EULAR/ERA-EDTA definitions as proteinuria < 0.5 g/day and normal renal function. Clinical-demographic characteristics at baseline were compared using survival analysis for time-to-CCR. Variables with $p < 0.25$ on univariate analysis with Log-Rank tests and lupus nephritis histological class (III/IV) were further evaluated as potential predictors with multivariate Cox proportional hazards regression models (Backward Stepwise method) adjusting for potential confounding.

Results 56 patients were included in the analysis (76.8% female, age at baseline 30.0 ± 13.2 years-old). Over the follow-up period, 51 patients (91.1%) reached CCR, within a median time of 6.0 months. High blood pressure ($p = 0.047$), no hydroxychloroquine therapy ($p = 0.012$), induction treatment with cyclophosphamide (as compared to mycophenolate mofetil - MMF) ($p = 0.027$) and proteinuria > 2 g/day ($p = 0.008$) were associated with longer time to CCR in univariate analysis. In multivariate analysis, proteinuria > 2 g/day at baseline (HR 2.651; 95%CI 1.338–5.25; $p = 0.005$) was a predictor of worse renal outcome, while induction therapy with MMF lead to shorter time to CCR as compared with cyclophosphamide (HR=0.525; 95%CI 0.277–0.998; $p = 0.049$). Other variables lost significance and were not included in the final model. The addition of glucocorticoid pulses and/or antihypertensive drugs to induction therapy did not influence renal outcome.

Conclusions Most of the patients reached CCR during the follow-up period. Proteinuria above 2 g/day at baseline and use of cyclophosphamide as compared to MMF induction were associated with worse renal outcome.

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EARLY AND SUSTAINED RESPONSES WITH ANIFROLUMAB IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN 2 PHASE 3 TRIALS

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Background In the phase 3 TULIP-2 and TULIP-1 trials in SLE, anifrolumab treatment increased the percentages of patients with BICLA responses vs placebo at Week 52 (Morand *et al*, 2020; Furie *et al*, 2019). To better understand the time course of BICLA responses to anifrolumab, we examined responses over time in TULIP-2 and TULIP-1, including sustained responses.

Methods The TULIP-2 and TULIP-1 randomized, double-blind, placebo-controlled trials evaluated anifrolumab (300 mg Q4W) over 52 weeks in patients with moderately to severely active SLE receiving standard-of-care treatment. Time to onset of BICLA response sustained from attainment through Week 52 was assessed.

Results At the first 3 assessments (Weeks 4, 8, and 12) in TULIP-2, numerically greater percentages of anifrolumab-treated patients (26.8%, 35.3%, and 42.9%, respectively; N=180) had a BICLA response compared with placebo (21.3%, 21.6%, and 31.8%; N=182). A similar trend was observed in TULIP-1 with anifrolumab (23.3%, 34.2%, and 36.5%; N=180) vs placebo (18.3%, 23.2%, and 27.5%; N=184). Time to onset of BICLA response in patients who achieved sustained BICLA