S1A:4 ROBUST STRATIFICATION OF LUPUS BASED ON LONGITUDINAL GENE EXPRESSION DATA AND DISEASE ACTIVITY PATTERNS

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Introduction The heterogeneous clinical presentation of SLE is characterised by the unpredictable appearance of flares and remissions of disease activity associated with organ damage and severe symptomatology. Various attempts to classify lupus clinically have not been successful, still burdened by delayed diagnosis and clinical trial failures. Our aim was to develop and validate a robust method to reproducibly stratify patients with lupus according to longitudinal patterns of disease presentation and gene expression data obtained at several points in time.

Methods We calculated correlations among expression values of each gene and SLEDAI across the different time points for each patient. With these, we constructed a bi-dimensional inter-patient matrix. We developed a new approach to select genes strongly correlated with SLEDAI in absolute values across all patients as best genes to stratify patients and filter out the remaining. Finally, we obtain the stratification groups applying consensus clustering that estimates the probability of a patient to belong to a given cluster by random seed permutation.

Results Longitudinally, lupus patients group into three clusters. The three clusters shared the same mean SLEDAI and had no differences in the clinical parameters comprising the score. Functionally however, the clusters had clearly differentiated gene expression profiles and cellular profiles representing three different mechanisms of disease progression. We tested the stability of the clusters by different validation methods and obtained a high reproducibility and robustness. Our stratification method could be used in the future to establish and re-design lupus clinical trials and treatment, and may be used in any disease with measurable but variable patterns of disease progression. This work has received support from the EU/EFPIA/Innovative Medicines Initiative Joint Undertaking PRECISESADS grant n°1 15 565.

S1A:6 MCTD AND SLE: SIMILARITIES AND DIFFERENCES

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Background SLE and MCTD are both chronic immune mediated systemic diseases with similar clinical features. We wanted to compare characteristics and morbidity in addition to mortality prediction models in our large and population based cohorts of SLE and MCTD.

Method 243 SLE patients from the Oslo SLE cohort and 145 patients from the Norwegian MCTD cohort were included in the study. Clinical features were based on questionnaires and medical records in the SLE cohort and examination by protocol in MCTD patients. Vital status at the end of the study was obtained from the National Population Register of Norway. Cox regression analyses were used to find the predictive factors of mortality. Variables at a significant level of P less than 0.25 where considered a candidate in the prediction model by manual backward elimination procedure in addition to known mortality predictors.

Results SLE patients were more often affected by nephritis and leukenopia, while the proportion of Raynaud’s phenomenon and Interstitial Lung Disease (ILD) was larger in MCTD (table 1). More males were diagnosed with MCTD. 25 patients died in the SLE cohort after a mean follow-up of 9 (2) years. 26 patients died in the MCTD cohort after a mean (SD) follow-up of 10 (3) years. Predictors of mortality in multivariable analyses were Lupus Nephritis class III to VI, and Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterised by organ damage and severe symptomatology. The heterogeneous clinical presentation of SLE is predictable by the unpredictable appearance of flares and remissions of disease activity associated with organ damage and severe symptomatology. Various attempts to classify lupus clinically have not been successful, still burdened by delayed diagnosis and clinical trial failures. Our aim was to develop and validate a robust method to reproducibly stratify patients with lupus according to longitudinal patterns of disease presentation and gene expression data obtained at several points in time. We calculated correlations among expression values of each gene and SLEDAI across the different time points for each patient. With these, we constructed a bi-dimensional inter-patient matrix. We developed a new approach to select genes strongly correlated with SLEDAI in absolute values across all patients as best genes to stratify patients and filter out the remaining. Finally, we obtain the stratification groups applying consensus clustering that estimates the probability of a patient to belong to a given cluster by random seed permutation.
having had a myocardial infarct, stroke or Transient Ischemic Attack after adjustments to age, gender and disease duration (Table 2). The predictors of mortality in the MCTD cohort were %ILD of Total Lung Volume after age and gender adjustments (Table 3). According to the Harrell’s C index, patient outcomes were accurately predicted by the SLE multivariable model 85% of the time and 84% in the MCTD model.

Conclusions SLE and MCTD are similar in many aspects, but differ in disease manifestations that have an impact on mortality, indicating that different follow-up approaches and management is needed.

S1d: Therapeutic strategies

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Objective To evaluate the prevalence of different definitions of remission and their effect on damage in systemic lupus erythematosus (SLE).

Design and method We considered 293 caucasian SLE patients followed-up for 7 years (2009–2015): 253 (86.3%) were female, mean ±SD disease duration 11.1±7.8 years. Disease activity was assessed by clinical SLEDAI-2K (c-SLEDAI) and damage by SLICC/ACR Damage Index (SDI). We evaluate the effect of different definitions of remission (c-SLEDAI=0; c-SLEDAI £ 1; c-SLEDAI=0 and prednisone £ 5 mg/day; c-SLEDAI £ 1 and prednisone £ 5 mg/day; c-SLEDAI=0 and PGA <0.5; c-SLEDAI £ 1 and PGA <0.5; c-SLEDAI=0 and prednisone £ 5 mg/day and PGA <0.5; c-SLEDAI £ 1 and prednisone £ 5 mg/day and PGA <0.5) and different durations of remission (1, 2, 3, 4, 5 consecutive years) on SDI using multiple logistic regression analysis.

Results Frequency of remission achieved during the 7 year follow-up are reported in Table 1 according to the different definitions. The mean increase in SDI and the percentage of patients with increased of SDI from the baseline to the end of follow-up were significantly higher in unremitted and 1 year remitted patients compared with patients with 2-, 3-, 4- and ≥5 year remission, irrespective of the definition of remission. 5 year remitted patients had lower damage compared with 2 year (p<0.01) and 3 year (p<0.01) remitted patients. At multivariate analysis, a remission lasting at least 2 years was an independent predictor of no damage accrual only in the definitions including prednisone intake £5 mg/day and/or PGA <0.5 (Table 2).