BIOLOGICAL DMARDS-INDUCED LUPUS IN PATIENTS MINING FOR COMMON REACTIVITY PATTERNS OF LUPUS

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results were systemati-
guidelines.

Results

Clinical significance and therapeutic implications of ANA/anti-
body profiles (antinuclear (ANA), anti-dsDNA) were systemati-

Overall, ANA seroconversion was demonstrated in 14.22% (35/246), while anti-dsDNA in 8.94% (3/35) patients; statistical signifi-
cative negative correlation LVEF – disease duration and activity (p<0.05) was found. LV diastolic dysfunction as subclinical cardiac involvement was registered in 59.50% SLE, with a direct correlation with disease duration (p<0.05), but not with disease activity (SLEDAI) and organ damage (SLIC/ACR) (p>0.05). Global hypokinesis on TTE as an indicator of sub-
clinical myocardiitis was demonstrated in up to one third SLE, while cardiomyopathy in one fourth. Mild pericardial effusion is observed in 31.2% cases, while cardiac tamponade in 4 cases; pericardial thickening was reported in 38% SLE. Finally, abnormal systolic pressure in pulmonary artery was found in 24.79% patients.

Conclusion

Patients with SLE are at increased risk to develop either clinical or subclinical cardiovascular manifestations as demonstrated by echocardiographic studies. A systematic TTE assessment is routinely recommended for the screening and monitoring of cardiac events.

Biological drugs (bDMARDs) have changed landscape and outcomes in various rheumatic conditions. Increased risk for infections, paradoxical reactions, autoimmunogenicity are widely acknowledged and may be responsible for treatment failure and switching among biologics.

Objective

To assess drug-induced autoimmunity (serology, clinical significance) in patients with rheumatoid arthritis (RA) treated with bDMARDs.

Patients and methods

Longitudinal observational study in 246 bionaive RA receiving their first bDMARD, anti-tumour necrosis factor (TNF) or non-TNF drugs, according to local treatment guidelines.

Disease activity, therapeutic response and serial autoantibody profiles (antinuclear (ANA), anti-dsDNA) were systematically assessed at baseline and every six months. Prevalence, clinical significance and therapeutic implications of ANA/anti-dsDNA specificities were further analysed (SPSS-19, p<0.05).

Results

214 RA received TNF inhibitors (56 infliximab, 65 adalimumab, 8 golimumab, 18 certolizumab, 67 etanercept) as first bDMADs and 32 different mechanism of action (10 rituximab, 7 abatacept, 15 tocilizumab). Overall, ANA seroconversion was demonstrated in 14.22% (35/246), while anti-dsDNA in 8.94% (22/246); no change in the immunological profile under golimumab, certolizumab, abatacept or rituximab.

Significantly higher rates of ANA were reported in infliximab-treated RA (30.53%) as compared to adalimumab (18.46%), etanercept (7.46%) and tocilizumab (6.66) (p<0.05); anti-dsDNA positivity was found in 10 infliximab (17.85%), 4 adalimumab (12.30%), 3 etanercept (4.47%) and one tocilizumab (6.66%), within an average of 36.5 (2–67) months.

ANA/anti-dsDNA positive status correlated with RA activity (DAS28-ESR) and loss of therapeutic response, concomitant DMARDs (leflunomide) and corticosteroids, administration adverse reactions (p<0.05).

Only four patients (1.62%; 4/246) were classified as drug-induced lupus. Three of them (infliximab, adalimumab, tocili-

Purpose

Autoimmune diseases arise from an abnormal immune response of the body against self-proteins leading to tissue and organ damage. The excessive production of harmful autoantibodies (AAB) is a hallmark of autoimmune diseases including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and Sjogren’s syndrome (SJS). Also in cancer research, it has been recently shown that AABs are useful to characterise patients. The characterisation of patient subgroups by means of stratification is essential for the efficient development of therapies, but often difficult due to the lack of appropriate biomarkers. Personalised or precision medicine approaches rely on appropriate multivariate multiplexing technology and data analysis. AABs serve as diagnostic markers for various autoimmune diseases, but the co-occurrence of AABs has rarely been analysed and is difficult to comprehend. Detecting a broad set of AABs helps to investigate the similarity between patients. A multiplex signature enables clustering for the investigation of relationships and patterns, which can be related to relevant clinical variables.

Methods

Here, we illustrate Luminex bead-based AAB assays using a set of 96 biomarker targets and their utility to characterise SLE and SSc as well as cancer study groups.

Data analysis is based on bi-clustering algorithms and a prevalence and signature analysis of the markers. Cluster analysis was also performed using transformed data sets (qualitative to quantitative) for the investigation of relationships and patterns, which can be related to relevant clinical variables.
investigate and visualise characteristic marker prevalence and co-prevalence patterns.

**Results** Based on the individual marker pattern, patients can often be stratified belonging to different study subgroups. For example, for SLE we show that different reactivity groups exist including patients with different disease activity scores and organ damage patterns.

**Conclusions** We conclude that the approach of a comprehensive prevalence and signature analysis and a vivid data visualisation is useful for any multiplex omics assay.

**PS1:21** **URINARY MARKERS OF INFLAMMATION IN LUPUS NEPHRITIS PATIENTS**

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**Objectives** Renal involvement is the most important manifestation of systemic lupus erythematosus, but assessing of inflammatory response in kidneys with non-invasive methods is still challenging. In this study we aimed to define markers of active lupus nephritis (LN) using urine immune profiling.

**Methods** Levels of cytokines (18-plex array) and mRNA expression (40 immune and glomerular injury genes) were measured in urine samples of LN patients with active disease (n=17), during remission (n=16), and in healthy subjects (n=19).

**Results** Urine levels of CCL2, CCL5, CXCL10 and IL-6 were elevated in active LN as compared to remission (best discrimination for CCL2), and correlated with LN activity. In the active disease, urinary cell transcriptome showed strong upregulation of proinflammatory cytokines (e.g. TNF, CCL2, CCL5, CXCL10), Th1 related genes (e.g. CD3G, CD4, TBX21, IFNG), and markers of glomerular damage (NPHS2 [podocin]). Active pattern of gene expression was also observed in 5 patients in remission, who had moderately increased urinary leukocyte count, two patients from this group (40%) developed renal exacerbation during following 3 months. Markers of Th17 immune axis (e.g. IL-17A) were not observed in 5 patients in remission, who had moderately increased urinary leukocyte count, two patients from this group (40%) developed renal exacerbation during following 3 months.

**Conclusions** Active LN patients (also patients at risk of exacerbation) were characterised by marked increase of proinflammatory mediators in the urine. We identified CCL2 chemokine as the most promising marker for monitoring of disease flare.

**PS1:22** **USE OF INTERFERON ALPHA AND INTERLEUKIN-10 AS CLINICAL ACTIVITY BIOMARKERS IN SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS**

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**Purpose** To analyse the association among INF1A, IL10 and BLyS levels and clinical activity in SLE.

**Methods** A cross-sectional, observational study of 142 patients diagnosed of SLE according to SLICC 2012 criteria and 34 healthy controls was performed. In patients a complete blood-test was made, and clinical data by personal interview was collected. We analysed the serum concentration of IL10, BLyS and INF1A by colorimetric methods. SLE patients were dichotomized as high and low levels for each cytokine based on the cytokine level above 2 SD of the mean in healthy controls. Biostatistical analysis with R (3.3.2.) was performed.

**Results** In our SLE patients we observed higher values of IL10, BLyS and INF1A than healthy controls (p<0.001, p=0.005 and p=0.043 respectively), showing an average values in patients of 13.39±27.73 pg/mL INF1A, 9.99±15.84 pg/mL IL10 and 1811.31±1757.81 pg/mL BLyS. The mean clinical activity measured by SLEDAI was 5.91±5.06.

**Statistical analysis** indicate that INF1A levels are correlated to IL10 levels (p=0.001) and BLyS levels (p=0.034). Due to this finding, we categorised SLE patients by low or high level of the three cytokines: 44 INF1A(-)IL10(-)BLyS(-); 61 INF1A(+)IL10(+)BLyS(-); 5 INF1A(+)IL10(-)BLyS(+) and 19 INF1A(+)IL10(+)BLyS(+) and 14 INF1A(+)IL10(+)BLyS(+). There is a high association of increased IL10-INF1A levels and the increased of clinical activity measured by SLEDAI score (p<0.0001), and to a lesser extent with increased IL10-INF1A-BLyS levels. Patients with high IL10-INF1A and IL10-INF1A-BLyS showed a significant rise in C3-C4 consumption (p<0.001 and p=0.001 respectively) and high anti-dsDNA (p=0.001 and p=0.002 respectively). Patients with increased INF1A-BLyS exhibited high anti-dsDNA (p=0.004) and ENA positivity (p<0.001). In addition, patients with increased levels of IL10-INF1A-BLyS showed ANAs (p<0.001) and antiphospholipid autoantibody positivity (p=0.004).

**Conclusions** The 69% of our SLE patients displayed almost one cytokine increased, being the INF1A the cytokine that mainly is increased. However, increased IL10 levels, irrespective of whether there is also increased levels of BLyS and/or INF1A, is the cytokine which best fits to clinical activity in SLE.

**Poster session 2: Autoantibodies, biomarkers and imaging (2), Environmental, epigenetics and genomics**

**PS2:23** **ANTI-C1Q ANTIBODIES IN TURKISH SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS**

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**Purpose** Anti-C1q has been shown to be associated with systemic lupus erythematosus (SLE) and disease activity of lupus nephritis in previous studies. We studied anti-C1q specificity for SLE versus rheumatic disease controls and healthy controls and the association with SLE manifestations in a single centre cross-sectional study.

**Methods** Demographics, disease information and blood samples were obtained during routine follow-up visits of patients attending Kocaeli University rheumatology outpatient clinic. There were 150 SLE patients (92% female, mean: 46 years). Control group had 85 rheumatoid arthritis patients, 16...