

232 **EARLY SEQUENTIAL COMBINATION THERAPY WITH MIZORIBINE AND TACROLIMUS IN SIXTY THREE PATIENTS OF LUPUS NEPHRITIS IN A SINGLE CENTRE IN JAPAN**

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Background and aims Mizoribine is an inhibitor of inosine monophosphate dehydrogenase, which is widely used for patients with lupus nephritis and also patients after renal transplants. Its anti-cytomegaloviral effect is unique as an immunosuppressant. We examined the efficacy and safety of early sequential combination of mizoribine and tacrolimus in lupus nephritis.

Methods Retrospective review of electric medical record was performed for all the 63 patients who received the combination therapy of mizoribine and tacrolimus and corticosteroids for induction or maintenance of lupus nephritis at St. Luke's International Hospital, Tokyo, Japan. For efficacy analysis, we extracted a series of change in serum creatinine, serum complement level, urine protein creatinine ratio, dose of corticosteroid. We further reviewed safety profile such as adverse events occurred during the use of multi-target therapy, drug survival rate, or reasons for discontinuing multi-target therapy in all patients. Complete remission of lupus nephritis was defined as a value of proteinuria <0.5 g/gCr, normal urinary sediment, serum albumin 3.5 g/dl and a normal value of serum creatinine.

Results Fifty six out of the sixty three patients (female:male=59:4, average age 37.4 years old) achieved complete remission in 6 months and there were only two relapses and both of them had Class V nephritis. At four months, the average urine protein creatinine ratio was 0.36 g/gCr, and the average dose of prednisolone was 9.9 mg/day. There were only three episodes of infections which required antibiotics administrations.

Conclusions Early sequential combination of mizoribine and tacrolimus seems to be effective and safe for lupus nephritis.

233 **DEFINING SUBSETS IN SLE: THE INTERPLAY AMONG IFN- λ 1, IFN- α AND TH17 AXIS CYTOKINES**

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Background and aims Interferon (IFN)- α s are pivotal in systemic lupus erythematosus (SLE), and type III IFNs (IFN- λ s) were recently also associated with SLE. We investigated levels of IFN- α and IFN- λ 1, and related cytokines in SLE patients and controls.

Methods We included 261 SLE patients and 261 population controls. All were examined and assessed for current organ manifestations and disease activity/damage using SLAM, SLE-DAI and ACR/SDI scales. Levels of IFN- λ 1, IFN- α , IL-17A, IL-23 and IP-10 were measured by ELISA.

Results IFN- λ 1 and IFN- α were detected in 29% and 44% of patients respectively, but their levels did not correlate. High

serum levels of IFN- λ 1 were positively associated with anti-nucleosome antibodies and lymphopenia, but negatively with musculoskeletal damage. Positive correlations between levels of IFN- λ 1, IL-17A and IL-23 were observed. Patients with high levels of these three cytokines had more disease damage, especially renal. High levels of IFN- α were associated with mucocutaneous disease, leukopenia, low complement, Ro/SSA and La/SSB, whereas vascular events and antiphospholipid antibodies (aPL) were uncommon.

We identified two subgroups with high disease activity: one double IFN- λ 1 and IFN- α high and another IP-10 high. The former had more neuropsychiatric manifestations, while the latter had more arthritis.

Conclusions Measurements of circulating IFN- λ 1 and IFN- α define SLE patients with different characteristics. Levels of IFN- λ 1 correlate with Th17 cytokines and identify a subgroup with more damage. Disease activity is associated with either upregulation of both type I and III IFNs, or independently with IP-10. Our findings could be of major importance when tailoring therapy for SLE patients with agents targeting IFN-pathways.

234 **PROINFLAMMATORY CYTOKINES (IL6, TNF α AND INTERFERON γ) IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR CLINICAL CORRELATION**

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Background and aims To study the levels of proinflammatory cytokines (IL6, TNF α , IFN- γ) in systemic lupus erythematosus (SLE) patients as compared to healthy control volunteers and to correlate the levels of cytokines with clinical features in Indian patients

Methods After obtaining Institutional ethical clearance and written informed consent, 88 consecutive SLE patients (newly diagnosed and those in remission) and 60 age and sex matched healthy controls were taken for the study, which was conducted between June to December 2015 in a tertiary care centre. Patients who had overlap syndromes, Mixed connective tissue disorder, antiphospholipid antibody syndrome, secondary Sjogrens syndrome, Lupus flare due to infections and offending drugs, were excluded. A thorough history, clinical examination, baseline biochemical and immunological investigations were done. Serum IL6, TNF α , IFN- γ were estimated in all patients and controls by ELISA. Statistical methods were done using SPSS software.

Results Serum interferon γ levels were higher in patients (mean \pm SD=25.65 \pm 64.81 pg/ml; median 8) than the controls (mean \pm SD=2.95 \pm 10.28 pg/ml, median-0), (p=0.0080). Serum IL6 levels were also higher in patients (mean \pm SD=143.01 \pm 64.94 pg/ml) than controls (mean \pm SD=69.33 \pm 11.7 pg/ml), (p<0.0001). Serum TNF- α were also elevated in patients (mean \pm SD=427.13 \pm 206.49 pg/ml; median 384.5) than controls (mean \pm SD=236.05 \pm 23.53 pg/ml; median 238), (p<0.0001). Interferon γ levels were significantly higher in females, lower in patients with lymphadenopathy and significantly higher in lupus nephritis class III, positively correlated with thrombocytopenia and negatively correlated with ESR, dsDNA, C3, C4. IL6 and TNF α were significantly associated with oral ulcer and alopecia respectively. Both showed a