The additive effects of hydroxychloroquine to maintenance therapy with standard of care in patients with systemic lupus erythematosus

Ippei Miyawaga, Kazuhisa Nakano, Shingo Nakayamada, Shigeru Iwata, Kentaro Hanami, Shunshu Fukuyo, Satoshi Kubo, Akio Kawabe, Yusuke Miyazaki, Yoshiho Inoue, Masanobu Ueno, Yoshiya Tanaka. University of Occupational and Environmental Health, Japan, The First Department of Internal Medicine, Kitakyusyu, Japan

Background: Antimalarial agents such as hydroxychloroquine (HCQ) have long been used as effective therapies for skin and joint symptoms, as well as for the malaise associated with cutaneous lupus erythematosus and systemic lupus erythematosus (SLE). Furthermore, based on the various benefits demonstrated with antimalarials, the use of antimalarials was recently recommended for all patients with SLE. Whereas HCQ has been generally given to most patients from the beginning of the treatment during the remission-induction therapy in multiple studies, its effects on maintenance therapy have not been sufficiently supported by evidence.

Objectives: We evaluated the additive effects of HCQ in maintenance therapy with standard of care (SoC) in 101 patients with SLE for 1 year.

Methods: The study included 101 patients diagnosed with SLE, whose course was followed for 1 year at our hospital and affiliated institutions. All patients were receiving maintenance therapy based on the SoC. The primary endpoint was the changes in the SLEDAI. The secondary endpoints were the proportion of emergence of new BILAG A or B organ domain score, and changes in anti-ds DNA Ab titre (U/mL), and serum complement activity (CH50, U/mL) up to year 1, as well as the CS-sparing effect. For these endpoints, the SoC+HCQ group (n = 42) was compared with the SoC group (n = 59) of patients matched for baseline characteristics. The Human Ethics Review Committee of our university reviewed and approved this study.

Results: In the SoC+HCQ group, the mean age was 42.2 years, and there were 3 male and 39 female. The mean disease duration was 157.9 months. In the SoC group, the mean age was 43.5 years, and there were 6 male and 53 female. The mean disease duration was 116.9 months. At baseline, no statistically significant differences between the two groups were observed in any baseline characteristics. The SLEDAI improved from 3.07 to 2.28 in the SoC+HCQ group, but significantly deteriorated from 2.73 to 4.8 in the SoC group. The CH50 levels, anti-ds DNA antibody titre, and concomitant CS dose were not significantly changed. The increase in the SLEDAI and concomitant CS dose after 1 year were all significantly greater in the SoC group, and the proportion of patients with SLEDAI flare was significantly lower in the SoC+HCQ group (4.76% vs 25.4%) (SLEDAI flare was defined as an increase of at least four points in the SLEDAI). Regarding the BILAG organ domain, there were no significant differences. SLEDAI flare were observed in 17 patients. When baseline characteristics were compared between patients with and without SLEDAI flare, HCQ was significantly more frequently used in patients without SLEDAI flare. In addition, univariate and multivariate logistic regression analyses were performed to identify the predictive factors for no SLEDAI flare. The univariate logistic analysis identified HCQ use, and immunosuppressant use with a P value of <0.3. Subsequently, multivariate logistic analysis was performed with these factors as dependent variables and identified the presence or absence of HCQ use as a predictive factor (P = 0.0041, odds ratio 6.66, 95% confidence interval 1.73–44.1). The retention rate of HCQ was 90.5%.

Conclusion: The comparison between the SoC+HCQ and SoC groups revealed that the addition of HCQ to maintenance therapy with low-dose CS for SLE is safe, and that HCQ was effective, not only for the suppression of disease activity based on the SLEDAI, but also for the prevention of the exacerbation of disease activity. Thus, the present study revealed that HCQ may be a useful mainstay for maintenance therapy based on SoC in patients with SLE.

FR0178  CLUSTER PROFILING OF PATIENTS IN A REAL-WORLD DATA SET WITH SYSTEMIC LUPUS ERYTHEMATOUS AND THEIR ASSOCIATED TREATMENTS

Zahi Touma1, Ben Hoskin2, Christian Atkinson3, David Bell4, Olivia Massey2, Jennifer H. Lofland2, Pam Berry4, Chetan Karyekar2, Karen Costenbader2
1University of Toronto, Toronto, Canada; 2Adelphi Real World, Cheshire, United Kingdom; 3Janssen Global Commercial Strategic Organisation, Horsham, United States of America; 4Janssen Global Services, LLC, Horsham, United States of America

Background: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations.

Objectives: To describe the presentation of SLE across different cohorts of patients and describe standard of care within clusters.

Methods: Cross-sectional study of 263 rheumatologists in the US and EUS. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Physicians completed patient record forms (PRFs) for the next 5 patients consulting with SLE; these patients completed self-completion (PSC) forms describing how SLE affected them. PRFs data include patient’s characteristics and management history. PSCs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Principal-component factor analysis reduced 39 unique SLE symptoms to 8 factors. These factors were used as covariates in latent class cluster analysis to provide discrete cohorts of patient. Chi-squared and Kruskal-Wallis tests compared discrete cohorts of patients. Cox and stratified Cox regression were used to describe patient outcomes across clusters.

Results: Data were extracted from 1376 PRFs. Factor analysis resulted in 8 clusters of concurrent symptoms; joint, haematological, constitutional, mental health, skin, circulatory, cardiovascular, renal, and muscular symptoms respectively. The four-cluster solution was selected. Cluster 1 displayed the lowest symptom burden, characterised by low skin involvement. Cluster 2 is characterised by joint and skin involvement. Cluster 3 & 4 had a high frequency of all factors, with cardiovascular involvement high in cluster 3 and renal/constitutional involvement high in cluster 4 (table 1).

Significant between-cluster differences were observed when comparing clinical and humanistic outcomes; physician/patient satisfaction were greatest in cluster 1 (physician satisfied 94.2% vs. 2: 90.8%, 3: 85.2%, 4: 74.4%, p<0.0001; patient satisfaction 94.7% vs. 2: 93.9%, 3: 91.5%, 4: 79.2%, p<0.0001), whilst disease progression (deteriorating slowly 2.5% vs. 2: 12.9%, 3: 9.8%, 4: 25.5%, p<0.0001) and flaring in the last 12 months (flared 30.0% vs. 2: 54.8%, 3: 62.2%, 4: 70.8%, p<0.0001) differed significantly with worst outcomes seen in cluster 4.

Significant differences were also observed between clusters in relation to treatment proportions; anti-malarials (highest cluster 1: 70.5%), biologic (highest cluster 3 & 4: 70.8%, 3: 9.8%, 4: 25.5%, p<0.0001) differed significantly with worst outcomes seen in cluster 4.

Conclusion: This study adds to the evidence demonstrating the heterogeneity of SLE experienced within distinct patient clusters. Significant proportions of SLE patients experience high symptom burden and low levels of satisfaction. Additional analysis to understand limited biologic use in more severe patients is needed.


FR0179  PREDICTION OF RESPONSE TO RITUXIMAB IN SLE USING A VALIDATED TWO-SCORE SYSTEM FOR INTERFERON

Adewunmi Alase1, Zoe Wigston1, Agata Burska1, Elizabeth Henson1, M.D., Yuzuafil M.D. Yusof1, John Reynolds1, The Masterplans Consortium2, Miriam Wittmann1, Ian N. Bruce2, Edward Vital1,1 Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; 2University of Manchester, Centre for Musculoskeletal Research, Division of Musculoskeletal and Dermatological Sciences, Manchester, United Kingdom; 3University of Manchester, The MASTERPLANS project Team, Manchester, United Kingdom

Background: Rituximab (RTX) is used for resistant SLE but clinical response varies. We previously validated two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) that improved prediction of clinical outcomes in SLE. IFN-Score-A included most commonly reported ISGs and predicted flares and glucocorticoid requirements. IFN-Score-B included ISGs that respond to multiple IFN subtypes and predicted development of SLE in At-Risk individuals. Diagnosis of SLE was associated with both scores, while only IFN-Score-B was elevated in RA. The British Society for Rheumatology Biologics Registry (BILAG-BR) collects samples for RTX-treated patients in the UK. MASTERPLANS is a consortium to identify predictors of drug response.

Objectives: To investigate whether IFN-Score-A and IFN-Score-B predict BILAG response to RTX at 6 months.

Methods: This is a preliminary analysis of the first RTX-treated patients in the BILAG-BR with complete data. Patients were recruited if they were starting a first cycle of RTX for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by >=1 grade in active BILAG-2004 systems with no worsening in other systems. Whole blood was collected into TEMPUS tubes and RNA extracted. IFN-Scores were measured using a custom Taqman array as previously described [El Sherbiny et al., 2018]. Multivariate logistic regression was used to test IFN-Scores and baseline clinical covariates as predictors of BILAG response at 6 months.

Results: Samples were available from 147 patients, of whom 84 had complete baseline and 6 month clinical data available and were included in this analysis. 40/84 (47.6%) patients had BILAG response at 6 months. In univariate and multivariate analysis, high IFN-Score-B expression was significantly associated with clinical response (see table 1).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Non-responders</th>
<th>Responders</th>
<th>Univariable OR (95% CI)</th>
<th>P</th>
<th>Multivariable OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, 95% CI)</td>
<td>40.5 (36.2,44.8)</td>
<td>40.9</td>
<td>1.015 (0.991,1.037)</td>
<td>0.188</td>
<td>0.994 (0.959,1.032)</td>
<td>0.765</td>
</tr>
<tr>
<td>Baseline organs affected</td>
<td>22/44</td>
<td>23/40</td>
<td>0.866 (0.468,1.601)</td>
<td>0.645</td>
<td>1.024 (0.381,2.750)</td>
<td>0.962</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>21/44</td>
<td>18/40</td>
<td>0.728 (0.392,1.354)</td>
<td>0.278</td>
<td>0.424 (0.145,1.244)</td>
<td>0.118</td>
</tr>
<tr>
<td>Renal</td>
<td>21/44</td>
<td>16/40</td>
<td>0.869 (0.471,1.070)</td>
<td>0.591</td>
<td>0.627 (0.162,2.391)</td>
<td>0.494</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>9/44</td>
<td>5/40</td>
<td>1.250 (0.532,2.824)</td>
<td>0.735</td>
<td>0.769 (0.170,3.473)</td>
<td>0.731</td>
</tr>
<tr>
<td>Neurological</td>
<td>7/44</td>
<td>6/40</td>
<td>0.859 (0.308,2.065)</td>
<td>0.735</td>
<td>0.769 (0.170,3.473)</td>
<td>0.731</td>
</tr>
<tr>
<td>Antimalarial-Yes</td>
<td>41/44</td>
<td>39/40</td>
<td>1.458 (1.015,1.863)</td>
<td>0.016</td>
<td>0.073 (0.005,1.005)</td>
<td>0.050</td>
</tr>
<tr>
<td>IFN-Score-A (per unit)</td>
<td>2.49 (1.77,3.19)</td>
<td>1.74</td>
<td>0.845 (0.682,1.048)</td>
<td>0.126</td>
<td>1.601 (0.935,2.743)</td>
<td>0.086</td>
</tr>
<tr>
<td>IFN-Score-B (per unit)</td>
<td>2.36 (1.98,2.73)</td>
<td>1.76</td>
<td>0.606 (0.394,0.933)</td>
<td>0.023</td>
<td>0.267 (0.093,0.762)</td>
<td>0.014</td>
</tr>
</tbody>
</table>