Long title: Outcomes following mycophenolate mofetil versus cyclophosphamide induction treatment for proliferative Juvenile-onset Lupus Nephritis

Short title: MMF vs IVCYC in Juvenile-onset LN

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Background: Patients with juvenile-onset Systemic Lupus Erythematosus (JSLE) experience more severe disease when compared to individuals with adult-onset disease. Despite differences in phenotypes and pathogenesis between age groups, treatment is based upon adult trials. We compared treatment response and outcomes in JSLE-associated lupus nephritis (LN) patients treated with mycophenolate mofetil (MMF) or intravenous cyclophosphamide (IVCYC).

Methods: UK JSLE Cohort Study participants with class III or IV LN were included, measuring treatment response, damage accrual, time to inactive disease and/or subsequent flare. Mann-Whitney U, Fisher's exact and Chi-squared tests utilised.

Results: 34/51(67%) received MMF and 17/51(33%) IVCYC. No significant differences in renal-BILAG scores, urine albumin/creatinine ratio, serum creatinine, ESR, anti-dsDNA-antibody, C3-levels, patient/physician global scores and prednisolone dosage were identified at 4-8, 10-14 months, and last follow-up. Standardised Damage Index scores did not differ between groups at 13 months, or last follow-up. Inactive LN was attained 8.5[4.5–12.6] months after MMF treatment, and 4.9[3.8-9.8] months following CYC (*p=0.17*). Time to renal flare was 14.5[5.1-40.8] months for MMF, and 11.1[6.4-20.5] months for CYC (*p=0.47*).

Conclusion: This is the largest study to date investigating induction treatments for proliferative LN in children, demonstrating comparability of MMF and IVCYC. Future randomized prospective studies are needed.

Keywords: Systemic Lupus Erythematosus, Lupus Nephritis, JSLE, SLE, Mycophenolic Acid, MMF, Cyclophosphamide.

Word count: 2597

Introduction

Juvenile-onset systemic lupus erythematosus (jSLE), also known as childhood-onset SLE, comprises approximately 15-20% of all systemic lupus erythematosus (SLE) cases. The underlying molecular pathophysiology, clinical presentations, and disease outcomes vary between JSLE and adult-onset SLE, with JSLE patients displaying a more aggressive disease course [1-3], including more renal involvement. Up 80% of JSLE patients develop Lupus Nephritis (LN) [1], compared with 40-50% of adult SLE patients [4, 5]. Overall, JSLE patients exhibit higher mean SLE disease activity index (SLEDAI) scores at diagnosis and over their disease course [2, 4, 5]. Furthermore, JSLE patients require more aggressive treatment, including greater corticosteroid and immunosuppressive treatment burden over time [2, 4, 5], and lastly experience more rapid accrual of disease related damage as compared to adult SLE cohorts [2, 5, 6].

Despite distinct differences in the phenotype and pathogenesis of JSLE [7], international recommendations for the treatment of JSLE [8] and juvenile LN specifically [9], are largely based upon data arising from clinical trials and observations in adult-onset SLE patients. As a consequence, head-to-head comparisons of induction treatments for proliferative, class III/IV International Society of Nephrology/Renal Pathology Society (ISN/RPS) LN in children are lacking. The largest paediatric study available retrospectively compared renal outcomes from seven patients treated with intravenous cyclophosphamide (IVCYC)

and six individuals treated with mycophenolate mofetil (MMF) [10]. This demonstrated a non-statistically significant trend towards more MMF treated patients achieving LN remission at six months. A randomized, open-label, non-inferiority trial including 140 North American adult SLE patients, suggested MMF to be more effective when compared to IVCYC [11]. Notably, in this study 56% of patients included were of Black race, and 17% were White. A further study including 370 adult SLE patients did not detect significant differences in renal response rates between patients receiving IVCYC vs. MMF for induction treatment [12]. A recent meta-analysis of available randomized trials in adults with LN (including 4,222 participants across 53 studies), demonstrated MMF, calcineurin inhibitors, or their combination to be most effective for inducing LN remission in adults, as compared to IVCYC [13].

The aim of this present study was to use observational data from the UK JSLE Cohort Study [1], to compare effectiveness of MMF vs. IVCYC induction treatments in patients with juvenile-onset LN, assessing response to treatment, damage accrual, time to achievement of inactive LN, and time to subsequent LN flare.

Materials and methods

Patients

Participants of the UK JSLE Cohort Study [1], recruited between 2006-2018, aged ≤16 years at the time of diagnosis and with ≥4 American College of Rheumatology (ACR) SLE classification criteria were included in this study if they had biopsy proven proliferative ISN/RPS class III or IV LN [14]. The majority of patients were recruited shortly after receiving a diagnosis of JSLE. However, at the time of the initial set-up of the cohort, previously diagnosed JSLE patients were recruited and retrospective data collected where possible. Patients were excluded from the current study where there was only a single study visit, no date documented on the study forms for when for the renal biopsy was undertaken, or where there was inadequate clinical data to calculate a renal BILAG score at the time of renal biopsy or over the first year post biopsy. The latter two exclusion criteria largely applied to patients who were diagnosed with JSLE prior 2006, when the UK JSLE Cohort started recruitment.

Patients with class III and/or IV LN were grouped according to whether they received MMF or IVCYC as induction treatment. Concomitant corticosteroid treatment was also documented (oral prednisolone, IV methylprednisolone (IVMP) or both). Self-reported ethnicity information was collected in accordance with the UK National Census categories [15]. Data from patients of mixed race were grouped with those of the associated ethnic minority group. Written patient assent/consent and parental consent was obtained to participate in the UK JSLE Cohort Study, and full ethical approval was in place from

the National Research Ethics Service North West, Liverpool East, UK (reference 06/Q1502/77). The research was carried out in accordance with the declaration of Helsinki.

Clinical data for assessing response to treatment

At a) baseline, b) 4-8, and c) 10-14 months post-biopsy, and d) the patient's last visit, renal parameters (urine albumin:creatinine ratio, serum creatinine and the renal domain of the BILAG score), global disease activity parameters (erythrocyte sedimentation rate (ESR), anti-double stranded DNA antibodies (ds-DNA), complement factor 3 (C3)) and patient/physician global scores (both 0-100 scale) were collected.

Assessment of LN disease activity and damage

The British Isles Lupus Assessment Grade (BILAG) score is a composite disease activity measure focusing on nine organs/systems (constitutional, mucocutaneous, neurological, musculoskeletal, cardiovascular/respiratory, renal, gastrointestinal, opthalmic and haematological). The BILAG score focuses on capturing disease transitions, with the clinician being asked to grade clinical features as new, the same, worse or improving over the last 4 weeks and as compared to the preceding 4 weeks, facilitating accurate assessment of new activity, flare, or remission in individual organs/systems [16]. The paediatric BILAG (pBILAG2004) has been adapted from the original adult BILAG score

[16] to include parameters of relevance to paediatric patients (e.g. normal blood pressure definitions), and has undergone validation in a UK paediatric cohort [17].

The renal domain of the pBILAG2004 disease activity score [1] was used to assess LN disease activity longitudinally. It is calculated using information on proteinuria, blood pressure, serum creatinine, glomerular filtration rate (GFR), active urine sediment, and recent renal biopsy findings. The renal pBILAG score is graded A-E and defined as follows; pBILAG2004 grade A/B: severe, moderate disease respectively, grade C patients: mild/improving renal disease, grade D: inactive disease but previous system involvement, grade E: system has never been involved [16]. The renal pBILAG score was used to define a change in LN activity; with attainment of inactive LN defined by the renal BILAG score changing from A, B or C to D; or subsequent flare following initial response to treatment defined by the renal pBILAG score changing from D to A or B. JSLE related damage was assessed using the Systemic Lupus International Collaborating Clinics Standardised Damage Index (SLICC-SDI) score [18] at 10-18 months post renal biopsy and last visit.

Statistical analysis

Renal parameters, laboratory markers of disease activity, renal pBILAG scores, patient/physician global scores and prednisolone dosage were compared between patients

who received MMF or IVCYC as induction treatment. Results are displayed as median values with interquartile ranges or counts and percentages. Since the data did not follow a normal distribution (Shapiro-Wilk test), non-parametric tests were employed. Mann-Whitney U tests were used for continuous data and Fisher's exact or Chi-squared tests for categorical data. All analysis was undertaken using PRISM version 6.0 software.

Results

At the time of data analysis (April 2018), the UK JSLE Cohort consisted of 411 patients meeting general inclusion criteria, with 69/411 (17%) experiencing proliferative LN (ISN/RPS class III or IV LN) during their disease course. Of these, 18/69 (29%) were excluded due to having only a single documented study visit (5/18 patients), or having insufficient clinical data at the time of their initial biopsy or over the first year of treatment (13/18 patients), leaving 51 patients who were subsequently considered (supplemental Table 1 displays the demographic details of the excluded patients). 34/51 (67%) received MMF (13/34 (38%) class III, 21/34 (62%) class IV LN), and 17/51 (33%) received IVCYC (8/17 (47%) class III, 9/17 (53%) class IV LN) as induction therapy (see Figure 1).

Of those individuals who received MMF induction treatment, 17/34 (50%) received concomitant oral prednisolone and the other 17/34 (50%) received both IVMP and oral

prednisolone. Within the IVCYC induction treatment group, 2/17 (12%) received oral prednisolone only and 15/17 (88%) received both IVMP and oral prednisolone. 32/34 (94%) of LN patients who received MMF induction treatment continued on MMF maintenance treatment. No patients received concomitant Rituximab at induction. 8/17 (47%) of those individuals who received IVCYC induction treatment subsequently received MMF maintenance treatment, 7/17 (41%) received azathioprine maintenance treatment and in 2/17 (12%) the maintenance treatment regimen was not documented.

Baseline clinical and demographic factors

There were no statistically significant differences between the groups receiving induction therapy with MMF or IVCYC in terms of clinical and demographic factors at baseline, including gender, ethnicity, age at diagnosis, age at LN onset, renal-pBILAG score, urine albumin/creatinine ratio, serum creatinine, ESR, anti-dsDNA antibody, C3 levels, patient/physician global scores and current prednisolone dosage (all $p>0.05$, see Table 1).

Response to treatment and damage accrual

No statistically significant differences were identified between the MMF and IVCYC induction treatment groups at either 4-8, or 10-14 months post renal biopsy, and last follow-up, in terms of renal-pBILAG score, urine albumin/creatinine ratio, serum

creatinine, ESR, anti-dsDNA antibody, C3 levels, patient/physician global scores and current prednisolone dosage (all *p>0.05,* see Table 2). The last follow-up visit occurred after a median of 4.2 years [2.2-7.2] for the MMF treatment group and 3.3 years for the IVCYC group [2.1-5.3]. JSLE-related damage did not differ between treatment groups after a median of 13 months [range 10-18 months] post renal biopsy, with median SLICC-SDI scores of 0 [0-1.0] in the MMF group, and 0 [0-2.5] in the IVCYC group (*p = 0.67*). Similarly, at the time of the last follow-up, no difference in SLICC-SDI scores were identified (MMF group = 1.0 [0-1.0], IVCYC group = 0 [0-2.5], *p = 0.90,* see Table 3).

Time to achievement of inactive LN and subsequent flare

A state of renal pBILAG-defined inactive LN (score = D) was reached in 29/34 (85%) patients who received MMF induction treatment and 14/17 (82%) patients who received IVCYC (*p = 1.00*). Inactive LN was achieved at a median of 8.5 months [4.5–12.6] after MMF treatment, and 4.9 months [3.8-9.8] following IVCYC treatment (*p = 0.17*). Similar proportions of patients experienced a subsequent LN flare (renal BILAG of D changed to A or B) regardless of the treatment group; 20/29 (69%) MMF treated and 7/14 (50%) IVCYC treated (*p = 0.32*). The time to subsequent flare was also comparable between the two patient groups; median of 14.5 months [5.1-40.8] for MMF treated, and 11.1 months [6.4-20.5] for IVCYC treated patients (*p = 0.47*).

Discussion

The aim of this study was to compare the effectiveness of MMF vs. IVCYC as induction treatments in children with LN, using data from the UK JSLE Cohort Study. Within the predominantly Caucasian JSLE study population, MMF and IVCYC had comparable efficacy with regards to treatment response, damage accrual, and time to next LN flare. Remission was reached sooner with IVCYC (median of 4.9 months following IVCYC and 8.5 months after MMF treatment). However, this did not reach statistical significance, warranting further analysis in larger studies. Of note, within this real-world UK-wide study, more patients received MMF than IVCYC as induction therapy for class III/IV LN (34/51 (67%) received MMF and 17/51 (33%) received IVCYC). The choice of LN induction treatment (MMF vs. IVCYC) was based upon individual physician's choice, with no specific guidelines on paediatric LN treatment in the UK. More patients in the IVCYC group received IVMP at induction when compared to the MMF group. However, oral prednisolone doses were comparable between groups at all time-points.

Results from the presented study highlight the need for a randomised and prospective comparison of MMF vs. IVCYC induction treatments, with strict steroid control between study arms, to better inform LN treatment protocols for children, especially given IVCYC's poor safety profile [11, 12]. Monitoring of serum MMF levels (e.g. through determination of AUC [19], with concentration-controlled dose adjustments is associated

with optimized mycophenolic acid exposure and an excellent renal outcome at 12 months of follow-up in a small sample of adult SLE patients with LN [20]. Therefore, monitoring of MMF levels may be considered within such a prospective study.

Observations of this study are complementary to findings reported by Lau *et al.* [10] who studied a much smaller cohort of American JSLE patients with class III LN (n=13), and demonstrated a comparable response following MMF or IVCYC induction treatment. The authors reported that 6 months after treatment initiation, no patient had achieved complete remission in the IVCYC group, while 57% were in partial remission. In the MMF group, 66% had achieved complete remission, 17% were in partial remission, and 17% were not in remission, leading to the conclusion that MMF may be superior to IVCYC for the induction of remission in LN at 6 months. Although, small patient numbers precluded any meaningful statistical analysis. The current study differs from reports of Lau *et al.* in that both class III and IV LN patients were included, and patient numbers allowed meaningful statistical analyses. In this regard, data presented here also support the Single Hub and Access point for Paediatric Rheumatology in Europe (SHARE) LN recommendations to use MMF as an induction agent for LN [9].

Results of the current study are also in-keeping with the reports from Appel *et al*. in adult SLE [12], the largest study to date comparing MMF vs. IVCYC induction treatment, albeit

in adult patients. It comprises a similar group of patients to the current study regarding race (US American; 39% White, 33% Asian, 27% 'other race' vs. 47% White, 35% Asian and 18% 'other' in the current UK JSLE Cohort Study). Also Appel *et al.* did not detect significant differences in renal response rates between IVCYC and MMF induction treatment [12]. Furthermore, no differences were seen between the MMF and IVCYC groups in relation to adverse events, or infections. We are unable to comment on this within the current study, since these data are not collected within the UK JSLE Cohort Study.

The study presented has several limitations which have to be considered. Despite being the largest JSLE study to date comparing response to MMF vs. IVCYC for LN induction treatment, patient numbers included are still relatively small. As per the inclusion criteria for this study, we only considered patients with class III or IV LN demonstrated on renal biopsy rather than all LN patients, for which these treatments are indicated, limiting the number LN patients available for inclusion. Unfortunately, almost one third of generally eligible patients had to be excluded, largely due to inadequate clinical data to calculate a renal BILAG score at baseline, or over the first year post renal biopsy. The UK JSLE Cohort Study collects patient data alongside routine clinical care. Therefore, reported clinical parameters, patient/physician global scores, treatment details and SDI damage data are recorded over a range of follow-up times post biopsy, rather than at exact

predetermined time points. Lastly, the length of follow-up varied somewhat between patient groups, with MMF treated patients being followed for a median of 4.2 years [IQR 2.2-7.2] and IVCYC patients for 3.3 years [2.1-5.3] (although this did not reach statistical significance).

The UK JSLE Cohort Study does not collect sufficient data to rigorously compare safety profiles of CYC vs. MMF treatments. In light of these limitations, prospective comparison of MMF vs. IVCYC induction treatment in larger, ethnically diverse JSLE cohorts, whilst monitoring treatment adherence (e.g. MMF levels) and drug safety data, would better inform treatment decisions for patients with LN.

Conclusions

This is the largest study to date investigating induction treatments for proliferative LN in JSLE. In a predominantly Caucasian JSLE populations, MMF and IVCYC appear to be comparably efficacious in regard to treatment response, damage accrual, and time to next flare. Randomized and prospective comparison of MMF vs. IVCYC treatment is warranted in ethnically diverse international JSLE cohorts to inform LN treatment protocols, and to explore the relative safety of both treatment regimens.

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Conflict of interest: The authors declare that there is no conflict of interest.

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Authors' contributions:

EMDS, MWB and CMH led on the conception and design of the study. ES performed the statistical analysis. All authors participated in the acquisition of and interpretation of the data. MWB is Chief Investigator of the UK JSLE Cohort Study. All authors were involved in drafting the manuscript and revising it critically for important intellectual content. They have also all read and given final approval of the version to be published.

Availability of data and material

Access to the data associated with this study can be requested by interested investigators by contacting the chief investigator of the UK JSLE Cohort Study Prof Michael Beresford (m.w.beresford@liverpool.ac.uk), on reasonable request.

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Table 1: Demographic and clinical details of the MMF and IVCYC treated groups at baseline

Demographics	**MMF induction (n=34)**	**IVCYC induction (n=17)**	***p-value***
Gender	F = 27 (79%) M = 7 (21%)	F = 14 (82%) M = 3 (18%)	*1.0*
Race			
• White British	16 (47%)	8 (47%)	
• Asian[a]	11 (32%)	7 (41%)	*0.81*
• African / Caribbean[b]	6 (18%)	1 (6%)	
• Other Caucasian origin	1 (3%)	1 (6%)	
Age at diagnosis (years)	12.6 [9.0-14.8]	13.3 [12.1-15.1]	*0.10*
Age at biopsy (years)	13.3 [11.2-15.0]	13.6 [12.8-15.6]	*0.20*
Renal pBILAG score	A – 9 B – 11 C – 1 D – 6	A – 4 B – 7 C – 2 D – 2	*0.69*
Urine albumin / creatinine ratio (mg/mmolCr)	45.5 [17.7-138.0]	177.8 [15.5-719.8]	*0.16*

Serum creatinine (μmol/l)	63.0 [51.0-137.0]	72.0 [57.8-101.5]	*0.18*
Patient global (0-100)	20.0 [2.0-25.0]	23.5 [0.0-55.5]	*0.86*
Physician global (0-100)	34.0 [11.0-50.0]	31.5 [9.4-40.0]	*0.82*
ESR (mm/h)	41.0 [11.0-80.0]	25.0 [10.0-56.75]	*0.64*
dsDNA (IU/l)	77.5 [26.5-270]	226.0 [200-400]	*0.15*
C3 (g/L)	0.86 [0.54-1.14]	0.85 [0.34-1.31]	*0.81*
Current prednisolone dose (mg)	28 [14-40]	25 [20-53]	*0.47*

[a]Asian origin included Bangladeshi, Indian and Pakistani patients. [b]African/Caribbean included patients of African, Caribbean, mixed White and Black African and mixed White and Caribbean origin. Counts and percentages or median values with interquartile ranges displayed. Mann-Whitney U tests used for continuous data Chi-squared tests for categorical data. Fishers exact test utilised to compare the proportion of active LN (renal paediatric British Isles Lupus Assessment Grade (pBILAG) domain A, B or C) to inactive LN patients (renal-pBILAG domain of D). MMF, Mycophenolate Mofetil. IV, intra-venous. CYC, Cyclophosphamide. F, female. M, male. ACR, American College of Rheumatology. ESR, erythrocyte sedimentation rate. DsDNA, anti-double stranded DNA antibodies. C3, complement factor 3.

Table 2: Comparison of JSLE clinical parameters and patient/physician global scores following MMF vs. IVCYC treatment.

Time post biopsy	Outcome parameter	MMF treated	IVCYC treated	*p-value*
4-8 months	**Renal pBILAG score[a]**	A – 3 (12%) B – 9 (35%) C – 3 (12%) D – 11 (41%)	A – 2 (14%) B – 2 (14%) C – 4 (28%) D – 6 (44%)	*1.0*
	Urine albumin / creatinine ratio (mg/mmolCr)	27 [12.8 – 96.4]	9 [1.3 – 67]	*0.46*
	Serum creatinine (μmol/l)	60.0 [47.5 – 75.0]	59.5 [49.8 – 75.0]	*0.86*
	Patient global (0-100)	10 [0 – 47.0]	16 [0 – 32.2]	*0.71*
	Physician global (0-100)	11 [1.5 - 25.5]	7.8 [5.0 – 31.5]	*0.71*
	ESR (mm/h)	10.5 [3.3-20.8]	23.5 [10.8 – 77.8]	*0.07*
	dsDNA (IU/l)	54.0 [29.6 – 88.9]	81.5 [0 – 270.0]	*0.84*
	C3 (g/L)	1.04 [0.87 -1.32]	0.88 [0.78 – 0.99]	*0.08*

	Current prednisolone dose (mg)	10 [10-15]	13 [8-23]	*0.48*
10-14 months	**Renal pBILAG score[b]**	A – 1 (4%) B – 5 (19%) C – 3 (11%) D – 18 (66%)	A – 1 (7%) B – 3 (21%) C – 2 (14%) D – 8 (58%)	*1.00*
	Urine albumin / creatinine ratio (mg/mmolCr)	13.25 [4.3 – 41.7]	20.5 [3.0 – 56.4]	*0.99*
	Serum creatinine (μmol/l)	59 [51.0 – 69.0]	62.0 [50.0 – 73.0]	*0.33*
	Patient global (0-100)	4.5 [0 – 9.3]	3.0 [0.5 – 52.0]	*0.98*
	Physician global (0-100)	7.0 [1.3 – 14.0]	9.9 [3.0 – 24.0]	*0.66*
	ESR (mm/h)	11.5 [5.0 – 20.8]	20.0 [4.0 – 48.5]	*0.62*
	dsDNA (IU/l)	44.0 [24.0 – 94.8]	20.4 [6.4 – 439.5]	*0.84*
	C3 (g/L)	0.98 [0.81 – 1.18]	1.04 [0.92 – 1.34]	*0.21*
	Current prednisolone dose (mg)	9 [5-10]	7 [4-14]	*0.89*
Last visit	**Renal pBILAG score[c]**	A – 1 (3%) B – 5 (16%)	A – 1 (7%) B – 1 (7%)	*1.0*

	C – 3 (9%) D – 23 (72%)	C – 2 (14%) D – 11 (72%)	
Urine albumin / creatinine ratio (mg/mmolCr)	21.0 [6.0 – 42.0]	17.4 [8.0 – 116.9]	*0.81*
Serum creatinine (μmol/l)	54.0 [46.0 – 59.0]	62.0 [50.5 – 74.8]	*0.08*
Patient global (0-100)	8.0 [0.0 – 30.0]	2.0 [0.0 – 52.0]	*0.75*
Physician global (0-100)	4.0 [0.0 – 15.0]	4.0 [0.0 – 23.5]	*0.56*
ESR (mm/h)	6.0 [3.0 -20.0]	15.0 [5.5 – 52.0]	*0.09*
dsDNA (IU/l)	51.3 [15.5 – 150.5]	14.5 [5.4 – 129.8]	*0.28*
C3 (g/L)	1.06 [0.92 – 1.24]	1.14 [0.83 – 1.21]	*0.94*
Current prednisolone dose (mg)	7 [5-9]	10 [5-20]	*0.42*

[a]Sufficient clinical data available to calculate the renal-pBILAG score in 26/34 MMF, and 14/17 CYC treated patients. Fishers exact test utilised to compare the proportion of active LN (renal-pBILAG domain A, B or C) to inactive LN patients (renal-pBILAG domain of D). [b]Sufficient data to calculate the renal-pBILAG score in 27/34 MMF treated and 14/17 CYC treated patients. [c]Sufficient clinical data to calculate the renal-pBILAG score in 32/34 MMF treated and 15/17 CYC treated patients. Median values/inter-quartile

ranges quoted for clinical parameters and patient/physician global scores. Counts/percentages given for renal-pBILAG scores. Mann-Whitney U test used to compare the treatment groups. MMF, Mycophenolate Mofetil. IV, intra-venous. CYC, Cyclophosphamide. pBILAG, paediatric British Isles Lupus Assessment Grade. F, female. M, male. ACR, American College of Rheumatology. ESR, erythrocyte sedimentation rate. DsDNA, anti-double stranded DNA antibodies. C3, complement factor 3.

Table 3: SLICC SDI damage scores at 10-18 months post renal biopsy and last follow-up visit.

Time	SLICC SDI		*p-value*
	MMF	**IVCYC**	
10-18 months post biopsy[a]	0 [0 - 1]	0 [0 – 2.5]	*0.67*
Last follow-up[b]	1.0 [0 – 1]	0 [0 – 2.5]	*0.90*

[a]SLICC SDI data available for 40/51 patients at 10-18 months post biopsy. [b]SLICC SDI data available for all 51 patients at last follow-up. Median values and inter-quartile ranges quoted, with Mann Whitney U test used to compare the treatment groups. SLICC-SDI, Systemic Lupus International Collaborating Clinics Standardised Damage Index score. MMF, Mycophenolate Mofetil. IV, intra-venous. CYC, Cyclophosphamide.

Supplemental Table 1: Demographic details of the excluded patients

Gender	F = 14 (77%) M = 4 (23%)
Race	
• White British	9 (50%)
• Asian[a]	5 (27%)
• African / Caribbean[b]	3 (17%)
• Other Caucasian origin	1 (6%)
Age at diagnosis (years)	11.0 [9.0-13.0]
Age at biopsy (years)[c]	12.1 [10.3-14.1]

[a]Asian origin included Bangladeshi, Indian and Pakistani patients. [b]African/Caribbean included patients of African, Caribbean, mixed White and Black African and mixed White and Caribbean origin. Counts and percentages or median values with interquartile ranges displayed. [c]Age at biopsy data not available for 3 patients.