Characteristics Associated With Use of the Lower Dose “EuroLupus” Cyclophosphamide Regimen in Youth with Proliferative Lupus Nephritis

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BACKGROUND
• Lupus nephritis (LN) is a common and serious complication of childhood-onset systemic lupus erythematosus (cSLE). Proliferative LN, defined as Class III or Class IV grading on lupus erythematosus (LE) classification criteria, requires aggressive immunosuppression to prevent development of end-stage kidney disease.

• Cyclophosphamide (CYC) is an alkylating agent commonly used to treat proliferative LN. Long-term risks (infertility, malignancy) are associated with cumulative dose.

• A lower dose “EuroLupus” CYC regimen demonstrated similar effectiveness for LN compared with the traditional higher dose “NHI” regimen in adults and is now standard of care; however, data in youth is lacking.

• To identify baseline demographic and clinical characteristics of youth treated with EuroLupus or NIH CYC regimens for proliferative lupus nephritis.

• To evaluate practice patterns of cyclophosphamide regimen use for youth with lupus nephritis from July 2014–June 2021.

METHODS
A retrospective cohort study was conducted at 11 N. American pediatric rheumatology centers that reported using the EuroLupus regimen ≥5 times in the past 6 years.

Patients were identified systematically through the EMR. Data were collected via chart review.

Inclusion criteria:
• Age < 22 years
• Met > 4/11 1997 American College of Rheumatology SLE classification criteria
• Received ≥ 1 dose of CYC to treat active proliferative LN from July 2014–June 2021

Exclusion criterion: dialysis use at CYC start

Demographic and clinical characteristics at CYC start (baseline) were compared using omnibus statistics.

To identify predictors of EuroLupus regimen (vs. NIH) CYC use, a multivariable generalized linear mixed model with logit link was fit using stepwise selection with a random intercept to account for correlation within sites.

RESULTS

**Table 1. Baseline demographics and clinical characteristics**

| Parameter                              | Total (n=161) | NIH (n=76) | EuroLupus (n=85) | p-value
|----------------------------------------|---------------|------------|------------------|--------
| Age at diagnosis of SLE, years, n=163 | 13.5±3.3      | 13.6±3.3   | 13.4±3.3         | 0.8143 |
| Age at diagnosis of lupus nephritis, years, n=163 | 14.4±3.2      | 14.2±3.2   | 14.7±3.2         | 0.2941 |
| Age at start of CYC course, years, n=153 | 15.1±3.3      | 14.6±3.3   | 15.8±3.3         | 0.1984 |

**Table 2. Predictors of EuroLupus regimen use**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate Model</th>
<th>Multivariate Model</th>
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<tbody>
<tr>
<td>Age at start of current CYC course, years</td>
<td>1.12 (1.02, 1.25)</td>
<td>0.019</td>
</tr>
<tr>
<td>Disease duration, years, n=125</td>
<td>1.25 (1.08, 1.46)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Female sex</td>
<td>1.87 (0.75, 3.56)</td>
<td>0.212</td>
</tr>
<tr>
<td>Race/Ethnicity, n (%)</td>
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<tr>
<td>White</td>
<td>0.8783</td>
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<tr>
<td>Hispanic/Latino</td>
<td>0.58 (0.31, 0.99)</td>
<td>0.0194</td>
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<tr>
<td>Asian</td>
<td>2.27 (0.81, 6.46)</td>
<td>0.1821</td>
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<tr>
<td>Black</td>
<td>0.60 (0.23, 1.58)</td>
<td>0.29 (0.06, 1.4)</td>
</tr>
<tr>
<td>Other</td>
<td>1.12 (0.75, 1.68)</td>
<td>1.07 (0.71, 1.62)</td>
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**Figure 1. Cyclophosphamide regimen use over time**

**CONCLUSIONS**

Among these 11 centers, use of the EuroLupus regimen for treatment of youth with proliferative LN is increasing, especially among female patients with longer disease duration.

Practice patterns around CYC dosing for youth with proliferative LN are evolving and further study is needed to assess outcomes between the two treatment regimens.

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References

