

ABSTRACT NUMBER: 047

Clinical Characteristics and Outcomes of North American Youth with Lupus Nephritis Requiring Dialysis Treated with Cyclophosphamide

Christine Wang¹, Rebecca Sadun², Wenru Zhou³, Kristen Miller³, Claire Palmer³, Stacy Ardoin⁴, Christine Bacha⁵, Emily Hause⁶, Joyce Hui-Yuen⁷, Nicole Ling⁸, Maria Pereira⁹, Meredith Riebschleger¹, Kelly Rouster-Stevens¹⁰, Aliese Sarkissian¹¹, Julia Shalen¹², William Soulsby¹³, Marinka Twilt¹⁴, Eveline Wu¹⁵, Laura Lewandowski¹⁶, Scott Wenderfer¹⁷ and **Jennifer Cooper**¹⁸, ¹University of Michigan, Ann Arbor, MI, ²Duke University, Durham, NC, ³University of Colorado, Denver, CO, ⁴Nationwide Children's Hospital, Columbus, OH, ⁵Akron Children's Hospital, Akron, OH, ⁶University of Minnesota, Minneapolis, MN, ⁷Cohen Children's Medical Center, Northwell Health, Lake Success, New York; Center for Autoimmune, Musculoskeletal, and Hematopoietic Diseases Research, Feinstein Institutes for Medical Research, Northwell Health, Manhasset, NY, ⁸UCSF, San Francisco, CA, ⁹Baylor College of Medicine, Houston, TX, ¹⁰Emory University/Children's Healthcare of Atlanta, Atlanta, GA, ¹¹UNC- Chapel Hill, Durham, NC, ¹²Johns Hopkins University, Baltimore, MD, ¹³University of California, San Francisco, San Francisco, CA, ¹⁴Alberta Children's Hospital, Calgary, AB, Canada, ¹⁵UNC Chapel Hill, Chapel Hill, NC, ¹⁶NIAMS, NIH, Bethesda, MD, ¹⁷British Columbia Children's Hospital, Vancouver, BC, Canada, ¹⁸University of Colorado/Children's Hospital Colorado, Denver, CO

Meeting: 2023 Pediatric Rheumatology Symposium**Keywords: cyclophosphamide, Lupus nephritis, Pediatric rheumatology, Systemic lupus erythematosus (SLE)**

SESSION INFORMATION

Date: Thursday, March 30, 2023**Session Type:** Poster Session A**Session Title: Posters: Clinical and Therapeutic I****Session Time:** 6:00PM-7:00PM

Background/Purpose: Few studies have evaluated the clinical characteristics and outcomes of youth with lupus nephritis (LN) treated with cyclophosphamide (CYC) who initially required kidney replacement therapy. CYC is partially renally cleared and the need for dose reduction with dialysis is controversial. Our study objectives were to summarize clinical characteristics of LN patients, describe treatment patterns, and compare the number of patients who required short-term dialysis versus those who developed end stage kidney disease (ESKD).

Methods: A multisite retrospective cohort study was conducted at 11 North American pediatric centers using electronic medical record data. Patients 6 to 22 years of age with active LN treated with either the lower dose EuroLupus (EL) or NIH CYC regimen from 7/1/2014 to 6/30/2021 were included. This subgroup analysis included patients who required dialysis at the time of CYC initiation (baseline). Patient data was collected at baseline, 3, 6, and 12 months. ESKD was defined as requiring dialysis therapy for >3 months. EL dosing was reviewed, and standard dosing was defined as 500 mg every 2 weeks for 6 doses, and any deviations from this dosing were recorded as modified. Baseline clinical characteristics and renal outcomes were summarized using descriptive statistics.

Results: Twenty patients met study inclusion criteria; of these, 15 (75%) received the EL regimen and 5 (25%) received the NIH regimen (**Table 1**). The average age at start of CYC during the study was 13.8 3.3 years. The cohort was predominantly female (75%), of diverse race/ethnicity, and publicly insured (60%). 80% of patients had new-onset LN while 20% had either relapsed or refractory disease. 95% of the cohort had proliferative LN and 30% had concurrent membranous disease. The mean cumulative dose of CYC was 5,823 mg 1,281 (NIH) and 2,681 mg 1,316 (EL). Of the 15 EL patients, 6 (40%) had modified dosing. Rituximab was given within 12 months of starting CYC to 40% of NIH regimen treated patients and 60% of EL treated patients. By 12 months, 3 patients (15%) had died, 4 (24%) met criteria for ESKD, and 13 (65%) had renal recovery off dialysis (**Table 2**). Of the patients with renal recovery, 11 of 13 (85%) were off before 3 months; 2 (15%) had an eGFR > 90 ml/min/1.73 m² at 12 months (**Table 2**). Infections requiring hospitalization during the CYC treatment period occurred in 1 (20%) patient who received the NIH regimen and 7 (47%) patients who received the EL regimen. 5 of 8 (63%) patients hospitalized due to infection also received rituximab.

Conclusion: A majority of youth with proliferative LN requiring dialysis at baseline had new-onset LN and were treated with a lower dose CYC regimen (standard or modified EL). Over half of the patients received concurrent rituximab. Although most patients were able to discontinue dialysis, almost a quarter developed ESKD, and 3 patients died. Limitations include small sample size, lack of data on dialysis indication or dialysis type, and a follow-up duration of only 12 months. There is also practice variation regarding CYC dosing modification for patients on dialysis and optimal dosing is unclear. Future larger prospective studies are needed to better understand outcomes for this vulnerable population.

Table 1: Baseline Demographics and Clinical Characteristics

	All (n=20)	NIH (n=5)	EL (n=15)
Age at diagnosis of SLE, years	13.1 ± 2.9	13.4 ± 3.2	13.0 ± 3.0
Age at diagnosis of LN, years	13.7 ± 3.4	14.0 ± 3.4	13.6 ± 3.6
Age at start of current CYC, years	13.8 ± 3.3	14.8 ± 3.5	13.4 ± 3.2
Female sex	15 (75%)	4 (80%)	11 (73%)
Race/Ethnicity			
Asian	2 (10%)	0 (0%)	2 (13%)
Black or African American	5 (25%)	2 (40%)	3 (20%)
Hispanic or Latino/a	7 (35%)	1 (20%)	6 (40%)
White	3 (15%)	1 (20%)	2 (13%)
Other ¹	3 (15%)	1 (20%)	2 (13%)
Insurance status			
Public	12 (60%)	3 (60%)	9 (60%)
Private	8 (40%)	2 (40%)	6 (40%)
Renal indication for CYC			
New-onset LN	16 (80%)	3 (60%)	13 (87%)
Relapsed or Refractory LN	4 (20%)	2 (40%)	2 (13%)
Complement 3 (C3) low	20 (100%)	5 (100%)	15 (100%)
Complement 4 (C4) low	18 (90%)	5 (100%)	13 (87%)
Sedimentation rate, mm/hr, n=17	60 (45 – 109)	54 (29 – 85)	67 (59 – 132)
Elevated blood pressure ²	17 (85%)	4 (80%)	13 (87%)
ISN/RPS Lupus Nephritis class			
Class II	1 (5%)	0 (0%)	1 (7%)
Class III	3 (15%)	0 (0%)	3 (20%)
Class IV	16 (80%)	5 (100%)	11 (73%)
Class V, concurrent	6 (30%)	2 (40%)	4 (27%)
Crescents present n=19	10 (53%)	3 (60%)	7 (47%)
Glomerulosclerosis present n=19	7 (37%)	2 (40%)	5 (33%)
TMA present	2 (10%)	1 (20%)	1 (7%)
NIH activity score ³ , n=15	9 (6 – 16)	12 (8 – 16)	7 (4 – 18)
NIH chronicity score ³ , n=15	2 (1 – 6)	2 (1 – 2)	2 (1 – 6)

Results are presented as mean ± standard deviation for normally distributed continuous data and median with interquartile range for non-normally distributed continuous data.

Counts with percentages are summarized for categorical data.

¹Includes Multi-Racial and Middle Eastern/North African patients

²Systolic blood pressure and/or diastolic blood pressure ≥ 95th percentile for age at baseline visit

³Modified NIH lupus nephritis activity and chronicity indices

Abbreviations: NIH = National Institutes of Health, EL = EuroLupus, SLE = Systemic Lupus Erythematosus, LN = Lupus Nephritis, CYC = Cyclophosphamide, ISN/RPS = International Society of Nephrology and the Renal Pathology Society. TMA = Thrombotic microangiopathy

Table 1: Baseline Demographics and Clinical Characteristics

Table 2: Outcomes of the Dialysis Cohort

	All (n=20)	NIH (n=5)	EL (n=15)
Three months			
Off dialysis, n (%)	11 (55%)	2 (40%)	9 (60%)
eGFR ¹ , ml/min/1.73 m ²	79 (63 – 111)	95 (n/a) ⁵	68 (59 – 111)
Urine protein:creatinine ratio ² , n=10	1.4 (0.7 – 4.3)	3.6 (n/a) ⁵	1.4 (0.4 – 3.4)
Death (cumulative)	2 (10%)	0 (0%)	2 (13%)
Six Months			
Off dialysis, n (%)	12 (60%)	3 (60%)	9 (60%)
eGFR ¹ , ml/min/1.73 m ² , n=12	84 (59 – 101)	103 (96 – 145)	63 (54 – 92)
Urine protein:creatinine ratio ² , n=11	0.6 (0.2 – 1.5)	1.3 (0.2 – 1.8)	0.6 (0.2 – 1.3)
End stage kidney disease, n=17	5/17 (29%)	2/5 (40%)	3/12 (25%)
Death (cumulative)	3 (15%)	0 (0%)	3 (20%)
Twelve Months			
Off dialysis, n (%)	13 (65%)	4 (80%)	9 (60%)
eGFR ¹ , ml/min/1.73 m ² , n=10	65 (57 – 100)	82 (57 – 146)	59 (57 – 85)
Urine protein:creatinine ratio ² , n=9	0.4 (0.2 – 1.3)	1.0 (0.2 – 1.9)	0.4 (0.1 – 0.7)
eGFR > 90 mL/min/1.73 m ²	2/13 (15%)	1/4 (25%)	1/9 (11%)
End stage kidney disease, n=17	4/17 (24%)	1/5 (20%)	3/12 (25%)
Death (cumulative)	3 (15%)	0 (0%)	3 ⁴ (20%)
Infection requiring hospitalization during CYC therapy ³	8 (40%)	1 (20%)	7 (47%)

Results are presented as mean ± standard deviation for normally distributed continuous data and median with interquartile range (IQR) for non-normally distributed continuous data. Counts with percentages are summarized for categorical data. Decreased “n” represent missing values.

¹GFR estimated using the modified Schwartz equation

²Units in mg protein/mg creatinine

³Infections included Cytomegalovirus viremia (2), invasive Aspergillosis (2), Enterococcus urinary tract infection, Streptococcus viridians bacteremia, septic shock of presumed infectious origin, febrile viral illness

⁴Two deaths secondary to invasive Aspergillosis, one unclear etiology

⁵Sample size (n=2) insufficient to calculate IQR

Abbreviations: NIH = National Institutes of Health, EL = EuroLupus, eGFR = estimated glomerular filtration rate, CYC = cyclophosphamide

Table 2: Outcomes of the Dialysis Cohort

Disclosures: C. Wang: None; R. Sadun: None; W. Zhou: None; K. Miller: None; C. Palmer: None; S. Ardoin: None; C. Bacha: None; E. Hause: None; J. Hui-Yuen: None; N. Ling: None; M. Pereira: None; M. Riebschleger: None; K. Rouster-Stevens: Accordant, 2; A. Sarkissian: None; J. Shalen: None; W.

Soulsby: None; **M. Twilt:** None; **E. Wu:** Enzyvant, 2, Pharming Healthcare, Inc, 2; **L. Lewandowski:** None; **S. Wenderfer:** Alnylam, 1, Bristol-Myers Squibb, 2, Novartis, 1; **J. Cooper:** None.

To cite this abstract in AMA style:

Wang C, Sadun R, Zhou W, Miller K, Palmer C, Ardoin S, Bacha C, Hause E, Hui-Yuen J, Ling N, Pereira M, Riebschleger M, Rouster-Stevens K, Sarkissian A, Shalen J, Soulsby W, Twilt M, Wu E, Lewandowski L, Wenderfer S, Cooper J. Clinical Characteristics and Outcomes of North American Youth with Lupus Nephritis Requiring Dialysis Treated with Cyclophosphamide [abstract]. *Arthritis Rheumatol.* 2023; 75 (suppl 4). <https://acrabstracts.org/abstract/clinical-characteristics-and-outcomes-of-north-american-youth-with-lupus-nephritis-requiring-dialysis-treated-with-cyclophosphamide-2/>. Accessed July 21, 2023.

ACR Meeting Abstracts - <https://acrabstracts.org/abstract/clinical-characteristics-and-outcomes-of-north-american-youth-with-lupus-nephritis-requiring-dialysis-treated-with-cyclophosphamide-2/>