Supplemental File: Survey questions that were distributed to the members of CARRA and PNRC. An asterisk (*) denotes questions where survey logic was utilized.

You are invited to participate in an educational study about IV cyclophosphamide prescribing patterns. Completion of this survey indicates your consent to participate. We will not know your identity unless you voluntarily choose to provide us with your name and contact information at the end of the survey; you can complete the entire survey without providing your name or contact information. All survey data will be analyzed in aggregate and will remain aggregated when presented. There are no risks involved with participating in this study. There will be no adverse effects if you decide to not participate. Participation is voluntary.

Background

1. Please describe your position:

- ◯ MD/DO faculty
- ◯ MD/DO fellow
- ◯ NP or PA practicing in pediatric rheumatology
- ◯ NP or PA practicing in pediatric nephrology
- ◯ Other (please specify)

2. If you are a MD/DO, what was your fellowship training program?

- ◯ Pediatrics (pediatric rheumatology, pediatric nephrology)
- ◯ Medicine **and** Pediatrics (combined rheumatology, combined nephrology)
- ◯ Other (please specify) or not applicable (please explain)

3. If you are medicine and pediatrics trained, which do you primarily practice?

- ◯ Pediatrics
- ◯ Medicine
- ◯ Both
- ◯ Not applicable

4. How many years have you been in practice post-fellowship?

5. What institution are you affiliated with?

6. Which of the following describes how most pediatric LN patients are seen at your institution?

7. Within your division, are LN patients seen by any of the providers, or only by a subset of providers, who are considered the institutional “lupus experts”?

- ◯ They are seen by any provider
- ◯ They are seen by only a subset of “lupus experts”

8. Would your colleagues identify you as a "lupus expert"?

- ◯ Yes
- ◯ No

9. What is your area of practice?

- ◯ Rheumatology
- ◯ Nephrology
- ◯ Other (please specify)

Background

* 10. Have you ever initiated treatment with IV cyclophosphamide for pediatric lupus nephritis?

- ◯ Yes
- ◯ No

For this survey, the NIH Cyclophosphamide Protocol, also known as "high-dose cyclophosphamide," is defined as IV cyclophosphamide 500-1000mg/m2, given once monthly for 6 consecutive months. For this survey, the Euro-Lupus Cyclophosphamide Protocol, also known as "low-dose cyclophosphamide" is defined as IV cyclophosphamide 500 mg (fixed dose) administered every 2 weeks for 6 doses (3 months).

11. What do you think may be the benefits of using the Euro-Lupus protocol compared to the NIH protocol? Please select all that apply.

- ☐ Decreased risk of infection
- ☐ Less post-infusion side effects (e.g., nausea)
- ☐ Lower risk of malignancy
- ☐ Less impact on future fertility
- ☐ Less IV fluid is required
- ☐ No need for mesna or leuprolide (Lupron)
- ☐ No need for nadir labs
- ☐ More acceptable to patients
- ☐ Easier to administer
- ☐ No benefit
- ☐ Other (please specify)

12. What do you think may be the downsides of using the Euro-Lupus protocol as compared to the NIH protocol? Please select all that apply.

- ☐ Insufficient data in pediatrics
- ☐ Insufficient data in African American and Hispanic patients
- ☐ I am not confident in efficacy compared to NIH protocol
- ☐ Every 2-week dosing difficult for patient (e.g. transportation, school and/or work absences)
- ☐ Increased risk of cytopenias and infection
- ☐ Fixed dose may not be appropriate for lightest/heaviest patients
- ☐ Fixed dose may not be appropriate given accelerated drug metabolism in children
- ☐ I am not sufficiently familiar with the protocol
- ☐ No downsides
- ☐ Other (please specify)

13. Please indicate your degree of agreement with the following statements.

	Strongly disagree	Disagree	Agree	Strongly agree
I am familiar with the cyclophosphamide dosing used in the Euro-Lupus protocol.	○	○	○	○
I am familiar with the other aspects of the Euro-Lupus protocol (requirements for fluids, lab monitoring, etc).	○	○	○	○

Personal Prescribing

* 14. Please estimate the number of times you have initiated treatment with IV cyclophosphamide (any protocol) for pediatric lupus nephritis over the last 12 months.

Personal Prescribing

* 15. Have you ever initiated treatment with the Euro-Lupus protocol for pediatric lupus?

- Yes
- No

Personal Prescribing

16. How do you feel your patients have responded to the Euro-Lupus protocol?

- ◯ Less well than NIH protocol
- ◯ Comparable to NIH protocol
- ◯ Better than NIH protocol

17. Have you ever started Euro-Lupus protocol but later decided the patient needed more cyclophosphamide?

- ◯ No
- ◯ Yes, so I switched in the middle of Euro-Lupus protocol to NIH protocol
- ◯ Yes, so I added extra NIH protocol doses after completion of Euro-Lupus protocol

Yes, other, please explain:

18. In what time frame do you expect to be able to assess patient response to Euro-Lupus protocol?

- ◯ Within the first six weeks (1-3 doses)
- ◯ Between weeks 6-12 (4-6 doses)
- ◯ 1-3 months after Euro-Lupus protocol completion
- ◯ >3 months after Euro-Lupus protocol completion

Euro-Lupus Use

* 19. Please estimate the number of times you have initiated treatment with the Euro-Lupus protocol for pediatric lupus nephritis over the last 12 months.

Euro-Lupus Use

For the next three questions, please answer for how you would dose Euro-Lupus cyclophosphamide for pediatric lupus nephritis:

20. Dose of cyclophosphamide:

- ○ 500mg fixed dose
- ○ Other, please explain

21. Frequency of infusions:

- ○ Q2 weeks
- ○ Other, please explain

22. Total number of infusions given:

- ○ 6 infusions
- ○ Other, please explain

23. If you are administering cyclophosphamide via the Euro-Lupus protocol, for which of the following would you modify the dose (select all that apply):

- ☐ I would not modify the dose; I always give a fixed 500mg
- ☐ I would decrease the dose for someone <50kg
- ☐ I would decrease the dose for someone with a substantial decrease in GFR
- ☐ I would decrease the dose for leukopenia
- ☐ Other (please specify)
- ☐ I would decrease for the following other reasons (please specify)
- ☐ I would increase for patients >120 kg
- ☐ I would increase for the following other reasons (please specify)

When you administer **Euro-Lupus** cyclophosphamide for pediatric lupus nephritis:

24. Do you give leuprolide (Lupron) or other GnRH agonist?

- Yes
- No
- Sometimes

25. Do you give mesna?

- Yes
- No
- Sometimes

26. Do you give >1L NS (pre-hydration + post-hydration total) with infusion?

- Yes
- No
- Sometimes

27. Do you check urine specific gravity for purpose of IV fluid administration?

- Yes
- No
- Sometimes

Prescribing Scenarios

28. How would you treat a patient in the following situations? Please assume a 70 kg 16-year-old girl with new-onset LN and 1 gram of proteinuria. After evaluating the patient, you have decided to give cyclophosphamide. Based on biopsy findings and renal function, which therapy would you initiate?

	Cyclophosphamide (Euro-Lupus)	Cyclophosphamide (NIH)
Class III, normal GFR	◯	◯
Mild/Moderate Class IV, normal GFR	◯	◯
Severe Class IV with normal GFR	◯	◯
Severe Class IV with impaired GFR	◯	◯

29. A 14-year-old girl presents to your clinic with malar rash, arthralgia, and fever. Laboratory testing reveals positive anti ds-DNA antibodies, reduced complement levels, elevated ESR, and abnormal urinalysis (500 mg/day protein, 25-50 RBCs/HPF). You diagnose this girl with SLE and decide to proceed with doing a kidney biopsy which reveals diffuse proliferative glomerulonephritis (class IV). Histological features compatible with very active inflammation are seen but there are no or minimal histological features of chronicity (damage). Typically, LN therapy is divided into "induction therapy" aimed at achieving complete response and "maintenance therapy" to help avoid renal flares. Which of the following medications would you use as induction therapy for this patient in addition to corticosteroids?

- ◯ Cyclophosphamide
- ◯ MMF
- ◯ Other (please specify)

30. Let's assume you decided on choosing cyclophosphamide for the patient in the last question. What dosing regimen would you choose, and please explain using the comment field why you picked that regimen.

- ◯ NIH protocol
- ◯ Euro-Lupus protocol
- ◯ Neither

Please explain your dosing regimen choice.

Prescribing: Special Populations

31. If you are planning to initiate cyclophosphamide for pediatric lupus nephritis, which of the following patient factors (if any) would lead you to choose Euro-Lupus protocol over NIH protocol? Select all that apply.

- ☐ High cumulative past exposure to cyclophosphamide
- ☐ History of serious recurrent infections
- ☐ Treated previously with cyclophosphamide and required dose reduction for cytopenias
- ☐ Other (please specify)
- ☐ Normal renal function
- ☐ I would never choose Euro-Lupus over NIH for any pediatric patient with lupus nephritis

32. If you are planning to initiate cyclophosphamide for pediatric lupus nephritis, which of the following patient factors (if any) would lead you to choose NIH protocol over Euro-Lupus protocol? Select all that apply.

- ☐ Impaired renal function
- ☐ High risk pathologic features on renal biopsy (e.g., crescents or tuft necrosis)
- ☐ Patient younger than 12 years
- ☐ Patient weight of < 50 kg
- ☐ Other (please specify)
- ☐ Patient weight of > 120 kg
- ☐ Non-Caucasian patient
- ☐ I would never choose NIH over Euro-Lupus for treatment of lupus nephritis

For the question below, only rheumatologists need answer...

33. Please complete the following table regarding using the Euro-Lupus protocol in the following conditions. Check all that apply.

	I have used it as first line	I would consider using it as first line	I have seen others at my institution use it as first line	I do not think it is appropriate for this indication
Lupus cerebritis	☐	☐	☐	☐
ANCA vasculitis	☐	☐	☐	☐
Diffuse alveolar hemorrhage due to underlying connective tissue disease	☐	☐	☐	☐
Macrophage activation syndrome due to underlying connective tissue disease	☐	☐	☐	☐
Interstitial lung disease due to underlying connective tissue disease	☐	☐	☐	☐

Other (please specify)

Institutional Practices

34. To your knowledge, how often are other colleagues within your division using the Euro-Lupus protocol for treatment of lupus nephritis when the decision is made to use IV cyclophosphamide?

- ◯ Never
- ◯ Rarely (<25%)
- ◯ Sometimes (26-74%)
- ◯ Primarily (>75%)
- ◯ I am unsure

Euro-Lupus Protocol Compared to NIH Protocol

35. Thank you for participating. Please feel free to tell us anything else about yourself, your cyclophosphamide prescribing practices, and your experiences with the Euro-Lupus protocol. If you are comfortable with us contacting you, please provide your e-mail.