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## Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage

### ReachMD Announcer:

You're listening to ReachMD. This medical industry feature titled "Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage" is sponsored by Aurinia Pharmaceuticals. Here's your host, Dr. Caudle.

### Dr. Caudle:

This is ReachMD, and I'm your host, Dr. Jennifer Caudle. Joining me to explore "Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage" are Dr. Maria Dall'Era and Dr. Tina Kochar. Dr. Maria Dall'Era is a rheumatologist and Chief of Rheumatology at University of California, San Francisco. Dr. Dall'Era, thank you so much for being here today.

### Dr. Dall'Era:

It's great to be here. Thank you for having me.

### Dr. Caudle:

Of course, we're excited that you're here. And Dr. Tina Kochar is a nephrologist and Associate Professor at the University of Texas Medical Branch in Galveston, Texas. Dr. Kochar, thank you for joining us today as well.

### Dr. Kochar:

Thank you for having me. Looking forward to an interactive discussion.

### Dr. Caudle:

Absolutely. Well, we're excited that you're both here. So to start us off, Dr. Dall'Era, can you please tell us about lupus nephritis, also known as LN, in patients with systemic lupus erythematosus, or SLE?

### Dr. Dall'Era:

Yes, systemic lupus erythematosus, I like to think of as the prototypic systemic autoimmune disease that can affect any organ system in the body. It is quite clinically and molecularly heterogeneous. The most common of the organ-threatening manifestations of systemic lupus is lupus nephritis. And what that means is that the kidneys are involved in the inflammatory and immune-mediated processes of systemic lupus. And this is very important; it's a manifestation that we actively look for—we screen our patients for—because it is associated with significant morbidity, as well as increased mortality in our patients with systemic lupus.

### Dr. Caudle:

Dr. Kochar, did you want to weigh in on that?

### Dr. Kochar:

When we see kidney involvement, as a nephrologist, it's very concerning because we need to make sure we diagnose these patients early on and treat them aggressively, so we can prevent any progression of their underlying kidney disease. Almost half of the SLE patients at some point can have kidney involvement. So, we need to be aware of the serious complication and diagnose these patients early on.

### Dr. Caudle:

Thank you for that. And, Dr. Kochar, why don't we stay with you for this next question. Are there any patient types that you're more worried about developing lupus nephritis?

### Dr. Kochar:

We know that lupus affects women of childbearing age more commonly. And we see that our younger patients have a more aggressive form of this disease. And also, we know that our minorities are affected more than others. So, we see that the disease is more aggressive in our Hispanic patients and African American patients. We need to educate the patients about this possible complication and diagnose these patients early on. So we need to preserve their kidney function early on and treat these patients accordingly.

**Dr. Caudle:**

So with that said, Dr. Dall'Era, did you have anything you'd like to add with that question?

**Dr. Dall'Era:**

I would just add that not only is there an increased incidence and prevalence of lupus nephritis among non-White populations, but there's an increased risk of progressive disease and the development of end-stage kidney disease in non-White populations, as well as in males and in pediatric-onset lupus. Studies have shown that those demographic factors not only lead to an increase in the incidence and prevalence of lupus nephritis, but worse outcomes as well.

**Dr. Caudle:**

Dr. Dall'Era, how do you talk to your patients about lupus nephritis?

**Dr. Dall'Era:**

When I have a patient with systemic lupus, it can be an incredibly overwhelming diagnosis to obtain, as you can imagine. We spend a lot of time talking about the potential for kidney involvement or lupus nephritis. Because we know that it's important to diagnose it early. And so, I talk to my patients about this. And I talk about how we screen for it—that it's very important to have these laboratories, including blood work, the urinalysis, the urine to protein to creatinine ratio done every 3 months—so we can make sure that we catch the onset of lupus nephritis early. So I step patients through that. And I think given the very busy lives of many of our patients, as Dr. Kochar said in the beginning, there is a striking, female predominance to this disease, childbearing age. Many of our patients are struggling with many responsibilities in life, including children, and trying to work, and sometimes going to school. Sometimes they can't physically get in to see a doctor every 3 months, but at least if they can go to the laboratory, and I can be monitoring those labs to make sure that nothing is popping up at those 3-month junctures—I think that's very important. And so, I stress the importance of this to our patients to make sure that these are being done.

And lastly, I spend time making sure patients realize that this is a chronic disease. Right now, we do not have a way of curing lupus nephritis or restoring tolerance in the kidney. But we do have a way of treating it and preventing progressive loss of kidney function. But setting that stage with patients and helping them realize that this is a long game: we're talking 3 to 5 years of immunosuppressive therapy. I think it just helps to manage expectations from the beginning: that we have to think about this as a long-term condition that we need to manage together over time.

**Dr. Caudle:**

For those of you who are just tuning in, you're listening to ReachMD. I'm your host Dr. Jennifer Caudle, and today, I'm speaking with Dr. Dall'Era and Dr. Kochar about "Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage."

Dr. Kochar, as a nephrologist, what's the importance of a timely renal biopsy?

**Dr. Kochar:**

A timely renal biopsy is indicated in majority of our patients where we suspect kidney involvement from SLE and mainly for two reasons. The first reason is that we want to confirm the diagnosis. Based on the clinical presentation, we usually have a fair idea that, yes, there is kidney involvement, but we want to be sure of the exact class of lupus nephritis based on kidney biopsy.

And the second main reason is for prognostic information, because a biopsy also helps us understand how much scarring they may have on the kidney biopsy, because that also helps with finalizing treatment decisions. Again, not every patient may be a candidate for immunosuppressive therapy. So it does depend on what we are seeing on the biopsy.

And at times, there can be delays in referrals. The key is really to get these patients into our clinics as early as we can, so when we do suspect kidney involvement, we can go ahead, plan the biopsy.

**Dr. Dall'Era:**

I completely agree. And I also love what Dr. Kochar mentioned about knowing how much, for instance, chronicity, how much fibrosis has already accumulated, because we're entering an era now where we're doing more repeated biopsies over time. And we can follow things like the Chronicity Index over time, and also the Activity Index over time. And the only way to know those parameters is with the kidney biopsy.

**Dr. Caudle:**

Excellent points. And to follow up, Dr. Kochar, can you please explain the reason for this impact on the kidney?

**Dr. Kochar:**

Yes, absolutely. So we know from studies that the longer these patients remain proteinuric, the worse the kidney outcomes. And kidney survival goes down significantly the longer these patients remain proteinuric. So our goal is to bring these patients into partial or complete remission as early as we can and with the lowest dose of steroids. Our goals now are much more aggressive for reductions in proteinuria. So, we really aim to get these patients into partial remission in less than 3 to 6 months, and in complete remission within a year. And this is what is also recommended by our society guidelines, the EULAR/ERA-EDTA guidelines, and KDIGO guidelines have similar recommendations.

**Dr. Dall'Era:**

And adding on to what Dr. Kochar just stated, proteinuria itself is not only a marker of glomerular wall injury, it's also an accelerant of disease because we know that when proteinuria gets into the tubules, the proteins get reabsorbed by the proximal tubular epithelial cells, which leads to an inflammatory response, which then leads to tubulointerstitial inflammation, and then fibrosis. And thus, the longer patients are living with proteinuria, and even low levels of proteinuria and albuminuria, the more progression they're going to have in their kidney disease. And so, it's vital to lower proteinuria as quickly as we can, early in the disease course, to prevent that fibrosis—that kidney damage that will be irreversible.

**Dr. Caudle:**

And now let's shift gears and take a look at treatment. Dr. Kochar, once you confirm a diagnosis and initiate treatment for lupus nephritis, what are your treatment goals?

**Dr. Kochar:**

So my goal is to start the treatment early. And now, we have newer therapies that are FDA approved. So our goal is to use what we call a multitarget treatment approach, where we use multiple drugs to target the proteinuria and to bring these patients into remission. Also, this helps us to lower the dose of steroids, because we know the longer these patients stay on steroids and high-dose steroids, the worst side effects they have. And these young patients, majority of them do not like the side effects of steroids. And that does affect compliance also.

In my own clinical practice now, I'm able to get these patients into some form of remission within 6 months, and with a significantly lower dose of prednisone 2.5 or 5 milligrams per day. So that's really my goal with these young patients.

**Dr. Dall'Era:**

And jumping in, that is exactly my goal as well. I think we're entering a time now of a paradigm shift in the treatment of lupus nephritis; wherein, we now have very good data from phase 3 trials of the newly approved therapies that we should be using combinations of therapies, multitargeted therapy, as mentioned by Dr. Kochar, early so we can attain an early complete renal response. It's a different paradigm than the way we've done things in the past—where we start with one therapy, one immunosuppressive for example, and we only escalate if a patient is getting worse—because we've learned that that takes a lot of time, and there was delays in treatment when we do that.

**Dr. Caudle:**

Before we close, I'd let to get some final takeaways from both of you on "Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage." Dr. Kochar, let's start with you.

**Dr. Kochar:**

The key is to diagnose these patients early, to ensure compliance, and to make sure the patients understand what's going on with their kidneys, and what we are following on to involve them in the care. And to make sure if they have family members or any other caregivers, they are on board because that really helps to have that support. And then once we have a treatment plan laid out, to make sure we start therapy as early as possible, prevent delays, get that biopsy taken care of.

So again, the theme here is to be aggressive in identifying kidney involvement in these patients and starting therapy early. Also, the emphasis now is also to reduce the dose of steroids as early as we can. And by using the newer therapies that I mentioned earlier that are now FDA approved, we are able to do that.

**Dr. Caudle:**

Excellent. And Dr. Dall'Era, I'll turn to you for the final word.

**Dr. Dall'Era:**

I think Dr. Kochar said everything beautifully. We want to make sure that we screen our patients effectively for the onset of lupus

nephritis. And we do this with every-3-month laboratories that we mentioned early. Once we suspect lupus nephritis, either because of a change in the urine sediment or an increase in proteinuria, or an unexplained decrease in eGFR, we get that kidney biopsy to make the diagnosis. As Dr. Kochar mentioned, we start with multiple therapies, with combination therapies, as demonstrated in our effective clinical trials, which led to the approval of our new agents. And the goal is to reduce that proteinuria quickly down to low levels—below that 0.5 level as quickly as we can. And because we have these new agents and these combinations, we have been able to use lower doses of glucocorticoids. And that's been very important because we know that any dose of glucocorticoid is associated with several risks: risks for organ damage, risks for cardiovascular disease, as well as just decreasing a patient's quality of life with the side effects that are involved with glucocorticoids.

**Dr. Caudle:**

That's a great comment for us to think on as we come to the end of today's program. I'd like to thank my guests Dr. Dall'Era and Dr. Kochar for joining us to take a look at "Proteinuria in Lupus: A Biomarker of Activity & an Accelerant of Damage." Dr. Dall'Era and Dr. Kochar, thank you so much for joining us today.

**Dr. Dall'Era:**

Thank you. It's been a pleasure.

**Dr. Kochar:**

Thank you very much.

**ReachMD Announcer:**

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