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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Insights on a Treatment Option for Lupus Nephritis

ReachMD Announcer:
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This medical industry feature, titled "Insights on a Treatment Option for Lupus Nephritis," is sponsored by GSK. This program is intended for US physicians.

Your host is Dr. Charles Turck.

Dr. Turck:
Biologics may impact the way we treat lupus nephritis. But where do they fit in the treatment landscape? And how do we implement them into our standard of care? This is ReachMD, and I'm Dr. Charles Turck.

Joining me today is Dr. Reinaldo Rosario, Clinical Assistant Professor at Florida International University. He's also a paid consultant to GSK. Dr. Rosario, thanks for being here today.

Dr. Rosario:
Thanks for having me.

Dr. Turck:
Before we dive in, I'd like to take a moment to share the indication and some important safety information for a biologic we'll be taking a look at today, BENLYSTA, also known as belimumab.

ReachMD Announcer:
BENLYSTA is indicated for patients aged 5 years and older with active systemic lupus erythematosus, SLE, or active lupus nephritis who are receiving standard therapy. BENLYSTA is not recommended in patients with severe active central nervous system lupus.

Important Safety Information.

BENLYSTA should not be administered to patients with a history of previous anaphylaxis with BENLYSTA.

Serious and sometimes fatal infections have been reported and occurred more frequently with BENLYSTA. Use caution in patients with severe or chronic infections, and consider interrupting therapy in patients with a new infection.

We'll continue to share additional important safety information throughout our program.

Dr. Turck:
We're going to start by getting right into treatment. Dr. Rosario, would you tell us about some key factors that inform your treatment choices for patients with lupus nephritis?

Dr. Rosario:
For lupus nephritis, we try our best to follow KDIGO guidelines. The initial treatment established with the KDIGO guidelines are steroids and immunosuppressants, such as MMF. At times, we can also use cyclophosphamide but it is less preferred in my practice. We've also used some tacrolimus, and now with a newer agents such as BENLYSTA, it gives us more options for the treatment of lupus nephritis. But we mainly follow guidelines and evidence-based treatment.

Dr. Turck:
Do you mind going into a little bit about the underlying causes of the disease?

Dr. Rosario:
Well it's an autoimmune disease. We've learned more about the disease and the role B cells play as the years have gone by. B cells play an active role in this process. Autoreactive B cells are a central driver of inflammation and damage to several organs in lupus and lupus nephritis. By binding soluble B lymphocyte stimulator called BLyS, BENLYSTA inhibits the survival of these B cells.

ReachMD Announcer:
The clinical relevance of these effects on B cells has not been established.

Dr. Turck:
Let's talk about the challenges of managing this disease. Would you share your experience with us?

ReachMD Announcer:
Treatment results may vary.

Dr. Rosario:
We've been treating lupus nephritis with the same regimens for the past 30 years. And if you look at the data, the chance of achieving remission is only about 20%. And of those, there is a high relapse in this condition. We've been looking to see what else can we do to improve outcomes and help minimize proteinuria and kidney disease progression.

I think that data that we have on newer agents like BENLYSTA, is great. And I feel that improves our chances of preserving kidney function for patients. We're focused on nephron conservation. The sooner we treat, the more kidney we can help save.

I think one of the challenges is patients' socioeconomic status. And these medications tend to be expensive. I think that's a big challenge for us, especially taking care of patients who have insurance difficulties.

And usually, as you know, this condition is quite complex. And as such, many patients have difficulty fully understanding it. In my practice, these patients tend to be skewed towards the young adults, for whom education is really, really important.

Dr. Turck:
Do you mind touching on the importance of earlier referrals and appropriate clinical intervention?

Dr. Rosario:
In my professional opinion, early intervention is the best disease mitigation strategy.

The sooner we take care of our patients, the better outcomes in terms of helping to avoid scarring of the kidneys, and helping to minimize the progression of kidney disease towards dialysis, or even mortality in those patients.

ReachMD Announcer:
Before we continue, here's some additional important safety information we need to be aware of.

Cases of JC virus-associated, Progressive Multifocal Leukoencephalopathy, or PML, resulting in neurological deficits, including fatal cases, have been reported. If PML is confirmed, stop immunosuppressant therapy, including BENLYSTA.

Acute hypersensitivity reactions, including anaphylaxis and death, and infusion-related reactions have been reported. Generally, reactions occurred within hours of the infusion but may occur later, including in patients who have previously tolerated BENLYSTA. Non-acute hypersensitivity reactions such as rash, nausea, fatigue, myalgia, headache, and facial edema, typically occurred up to a week after infusion. Monitor patients during and after treatment and be prepared to manage anaphylaxis and infusion-related reactions. Be aware of the risk of hypersensitivity reactions, which may present as infusion-related reactions. Discontinue immediately in the event of a serious reaction. With intravenous administration, if an infusion reaction develops, slow or interrupt the infusion.

Dr. Turck:
For those just joining us, this is ReachMD. I'm Dr. Charles Turck. And today I'm speaking with Dr. Reinaldo Rosario about the treatment of lupus nephritis.

How do you select a treatment for induction therapy? And how do you determine when it's time to transition to maintenance?

Dr. Rosario:
Mainly based on evidence-based guidelines. Standard therapy for lupus nephritis, in my practice, is induction and maintenance with mycophenolate and prednisone. For induction therapy, we tend to do a 24-week of high-dose standard treatment. And then we usually see our response and start maintenance therapy. That's what has been done historically. We follow evidence-based treatment recommendations, although now we have more methods and treatments. And that's what is changing and exciting in the treatment of lupus nephritis.

Dr. Turck:
How do you define failure on standard therapy?

Dr. Rosario:
I will say not seeing a significant reduction in proteinuria, not achieving a urine protein excretion less than 0.5, not achieving normal complement levels, and still having a positive ANA. It could be defined as a partial response. But for me, it's failure. Every nephrologist wants to minimize the urine protein as much as possible while protecting and preserving kidney function.

ReachMD Announcer:
Before we continue, here's some additional important safety information we need to be aware of.

Depression and suicidality were reported in patients receiving BENLYSTA. Before adding BENLYSTA, assess patients' risk of depression and suicide and monitor them during treatment. Instruct patients or caregivers to contact their HCP if they experience new or worsening depression, suicidal thoughts or behavior, or other mood changes.

There is an increased risk of malignancies with the use of immunosuppressants. The impact of BENLYSTA on the development of malignancies is unknown.

Live vaccines should not be given for 30 days before or concurrently with BENLYSTA as clinical safety has not been established.

Available data do not support the safety and efficacy of concomitant use of BENLYSTA with rituximab in patients with SLE. An increased incidence of serious infections and post-injection systemic reactions in patients receiving BENLYSTA concomitantly with rituximab compared to patients receiving BENLYSTA alone has been observed. The safety and efficacy of BENLYSTA concomitantly with other biologic therapies, including B-cell-targeted therapies, have not been established. Caution should be exercised if BENLYSTA is administered in combination with other biologic therapies.

Dr. Turck:
You've talked about the values indicative of treatment failure, but you know, the data show that despite immunosuppressive therapy, renal flares still occur. Would you speak more about that?

Dr. Rosario:
What we've done in the past, when there is a flare, we increased the steroid dose, which we've now learned how detrimental it is. That's what we've been taught, and I think that mentality should change. I think the goal has been to reduce the amount of steroids used.

And in my case, adding BENLYSTA to standard therapy earlier on, as appropriate, can help reduce the risk of renal flares and steroid use.

ReachMD Announcer:
Treatment results may vary.

Dr. Turck:
I'd like to focus on BENLYSTA as a treatment option for active lupus nephritis. Dr. Rosario, after selecting this medication for your patients, what kind of outcomes have you seen?

Dr. Rosario:
Well, we have data from the BLISS-LN trial in patients with active lupus nephritis, who were on BENLYSTA for up to 2 years. BENLYSTA has established efficacy and demonstrated significant improvement in renal response versus standard therapy alone at week 104. Moreover, the BLISS-LN trial, which is a 104-week trial, and by the way, the largest and longest phase 3 LN trial of a biologic, not only reveals a commitment to establishing the efficacy of the medication, but also its safety parameters.

It is important for me as a nephrologist to have long-term data too, as it is relevant to the care of lupus nephritis patients. I believe that the length of therapy of the BLISS-LN trial is one of its many strong points.

We need to understand that every patient is different and may have different treatment results. In my experience with BENLYSTA, I've seen a significant reduction in proteinuria, which is one of the main markers we follow.

One of the things that I tell my patients is that nobody loves their kidneys more than I do. And I will do everything possible to protect those kidneys as if they were mine. In most other diseases, we just prolong and delay the progression of kidney disease. But when we're dealing with lupus nephritis, it's something very rewarding to treat because we're able to feel like we're actually slowing damage progression. For us, it's very exciting to take care of our lupus nephritis patients with BENLYSTA, which has been shown to reduce the risk of renal flares.

ReachMD Announcer:
Treatment results may vary.

Before we continue, here's some additional important safety information we need to be aware of.

The most common serious adverse reactions in adult SLE clinical trials were serious infections; some were fatal. The most common adverse reactions, greater than or equal to 5%, were nausea, diarrhea, pyrexia, nasopharyngitis, bronchitis, insomnia, pain in extremity, depression, migraine, pharyngitis, and injection site reactions (with the subcutaneous injection).

Adverse reactions reported in clinical trials with SLE pediatric patients, age 5 years and older, and adult patients with lupus nephritis were consistent with those observed in adult SLE trials.

Dr. Turck:
What are some of the key considerations and challenges with keeping patients on BENLYSTA specifically for the treatment of active lupus nephritis?

ReachMD Announcer:
Treatment results may vary.

Dr. Rosario:
That's a very good question. Insurance coverage. I think the insurance aspect is a big, big challenge. My experience demonstrates that this medication works, and it has benefits. But if the insurance won't cover it, then that's a problem. Thankfully, GSK has programs and tools available to help providers and patients understand their coverage.

The key to keeping patients on therapy is education and putting our treatment expectations into context for our patients. As a physician, I am transparent about how their treatment is progressing, and that every patient reacts differently. For example, patients usually don't feel much when their protein improves. And they may say, 'You know, I mean, I don't feel anything. Why am I taking this?' We hear that all the time. So it's important to address that and explain to them when and how the treatments are working.

Part of setting expectations is reinforcing the importance of trying to avoid complications, like progressing to end-stage kidney disease. When we mention the word dialysis, it gets scary. When we tell patients that we need to minimize or significantly reduce the chances of them eventually being on dialysis, it's an eye opener, because they usually know someone who's been on dialysis. And they will say, 'No, no, I will never do that.' And we obviously don't want them to do it either. So we need to tell the patients that we'll work together to try to make sure that doesn't happen.

Dr. Turck:
So once a patient with lupus nephritis comes to your practice, however and whenever they've been referred to you, and you run through the tests, who's the BENLYSTA patient? Now how do you decide who's appropriate for BENLYSTA?

ReachMD Announcer:
Treatment results may vary.

Dr. Rosario:
Right now, I believe starting our active lupus nephritis patients during induction and continuing through maintenance, or our SLE patients whose disease is uncontrolled on standard therapy, are appropriate. However, we shouldn't forget that all patients are different, and we should always exercise our best clinical judgment.

Given the pros and cons of what has long been standard therapy, I think doing the same thing and expecting all of our patients to achieve remission, not acceptable. It's not acceptable. And as such, I use BENLYSTA with standard therapy for many of my patients with active lupus nephritis.

Dr. Turck:
Any thoughts about the dosing and administration of BENLYSTA for your patients?

Dr. Rosario:
Yes, each patient is unique with different needs regarding their administration route. It is important to give adult patients the options of the intravenous or subcutaneous form of administration. I always give them the option. But most of my patients have opted for the sub-Q form, so they can inject themselves at the comfort of their house. This was extremely helpful during the pandemia, in which many infusion centers in my area were closed.

Dr. Turck:

Would you talk a little bit about your experience in comanaging in the care of patients with lupus nephritis?

Dr. Rosario:
Usually, the rheumatologists treat SLE patients, and then as time goes by, these patients develop proteinuria. Some rheumatologists feel comfortable treating proteinuria, and some don't. So they refer early on. Many patients are referred to us for a kidney biopsy to see what kind of lupus nephritis they have and help them with the therapy. In my area, rheumatologists, for the most part, send us patients with SLE that have developed proteinuria. We go ahead and schedule and perform a kidney biopsy and help with the medical management of their lupus nephritis. We collaborate in treatment with immunosuppression to closely monitor for any type of adverse effects. It is in the patient's best interest, as you know, to have a multidisciplinary approach for their care, as this condition is very complex, and it affects multiple organs.

Dr. Turck:
Do you have any recommendations for nephrologists treating patients with active lupus nephritis with BENLYSTA?

Dr. Rosario:
Yes, I think the sooner we treat, the better. From my experience, I don't think that we should wait with standard conventional treatment and see if patients respond and then add it. I believe that BENLYSTA should be started during induction with standard therapy to help more patients achieve a renal response.

ReachMD Announcer:
Treatment results may vary.

Before we continue, here's some additional important safety information we need to be aware of.

There are insufficient data in pregnant women to establish whether there is drug-associated risk for major birth defects or miscarriage. After a risk/benefit assessment, if prevention is warranted, women of childbearing potential should use contraception during treatment and for at least four months after the final treatment.

HCPs are encouraged to refer patients and pregnant women are encouraged to enroll themselves by calling 1-877-311-8972 or visiting mothertobaby.org/ongoing-study/BENLYSTA-belimumab/.

BENLYSTA, belimumab, can be given as an I.V. infusion 120 milligrams per vial in patients aged 5 and older, or by subcutaneous injection 200 milligrams per milliliter in adults.

I would like to remind our audience that to report Suspected Adverse Reactions, contact GSK at 1-888-825-5249 or the FDA at 1-800-FDA-1088 or fda.gov/medwatch.

Please see full Prescribing Information and Medication Guide for BENLYSTA.

Dr. Turck:
Well, with those final considerations in mind, I want to thank my guest, Dr. Reinaldo Rosario, for joining us to discuss implementing BENLYSTA for the treatment of active lupus nephritis. Dr. Rosario, it was great speaking with you today.

Dr. Rosario:
Thanks for having me. My pleasure.

ReachMD Announcer:

Lupus Nephritis Study Design and Results
Study Design:
In a phase III study, 448 adult patients with active lupus nephritis were randomized to BENLYSTA plus standard therapy or placebo plus standard therapy. BENLYSTA 10 mg/kg or placebo was administered by IV infusion on Days 0, 14, and 28, and at 4 week intervals thereafter through week 104. Treatment failures were defined as patients who received prohibited medications.

Outcomes are defined as achieving renal response at Week 104 (primary endpoint), complete renal response at Week 104 (secondary endpoint), and time to renal related events or death (secondary endpoint).

Renal Response defined as eGFR $\geq$ 60 mL/min/1.73m^2 or no more than 20% below preflare value, uPCR $\leq$0.7 and not a treatment failure at Week 104. Significantly more patients on BENLYSTA (n=223) achieved renal response vs placebo (n=223); 43% vs 32%, respectively (P=0.0311).

This program was sponsored by GSK. If you missed any part of this discussion, visit ReachMD.com/industryfeature. This is ReachMD.

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