Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/medical-industry-feature/examining-clinical-data-for-a-lupus-nephritis-treatment/13883/

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

Examining Clinical Data for a Lupus Nephritis Treatment

ReachMD Announcer:
Welcome to ReachMD.

This medical industry feature, titled “Examining Clinical Data for a Lupus Nephritis Treatment,” is sponsored by GSK.

Here’s your host, Dr. Paul Doghramji.

Dr. Doghramji:
This is ReachMD, and I'm Dr. Paul Doghramji. This program is sponsored by GSK. Joining me to discuss the burden of lupus nephritis and share key clinical trial data is Dr. Dawn Caster, Nephrologist and Associate Professor of Medicine in the Division of Nephrology and Hypertension at the University of Louisville School of Medicine in Louisville, Kentucky. She's also sponsored by GSK. Dr. Caster, welcome to the program.

Dr. Caster:
Thank you so much. I'm very happy and excited to be here.

Dr. Doghramji:
We're thrilled to be here in Orlando, which has been an amazing opportunity to once again discuss strategies to improve the management of renal diseases with our peers.

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. Doghramji:
Let’s take a step back here and discuss the damaging effects of lupus nephritis.

Dr. Caster:
Yes, unfortunately, a substantial number of patients with lupus nephritis will experience kidney failure, with approximately 20% of patients with lupus nephritis progressing to end-stage kidney disease within 10 years of their diagnosis.

Dr. Doghramji:
How do renal flares play into the damage that leads to kidney failure?

Dr. Caster:

With each renal flare, there's potential irreversible nephron loss, which can shorten the lifespan of the kidney, increasing the risk of end-stage kidney disease.

Dr. Doghramji:
What do guidelines recommend for treatment? And how do patients typically respond to these therapeutics? Do the current standard treatments control renal flares?

Dr. Caster:
That's a great question. There are several guidelines available, including ACR and EULAR, for example.

The current guidelines recommend immunosuppressive therapy, either mycophenolate mofetil, or cyclophosphamide, and corticosteroids as initial standard therapy for patients with lupus nephritis.

However, it's been shown that those standard treatments have a high non-response rate, and are associated with both short- and long-term toxicities.

In a cohort of 145 patients with complete or partial remission, 45% developed renal flares over a mean of 117 months following withdrawal of pulsed cyclophosphamide with or without steroids. Renal flares are defined as a rise in serum creatinine level and/or proteinuria, abnormal urinary sediment, or reduction in creatinine clearance.

And again, continued flares mean continued potential nephron loss and increased risk of kidney failure. This highlights the need for treatments that are more effective and tolerable and that can help improve kidney outcomes.

ReachMD Announcer:
Before we continue, here is 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. Doghramji:
Now that we have some background on lupus nephritis, let's dive into the BLISS-LN clinical trial.

Dr. Caster, can you tell us a little bit about this trial?

Dr. Caster:
Absolutely. There's a lot to get into. Belimumab International SLE Study-Lupus Nephritis, or BLISS-LN, was a phase 3 study of 448 adult patients with active lupus nephritis who were randomized to either BENLSYTA plus standard therapy or placebo plus standard therapy.

Standard therapy included induction with either cyclophosphamide or mycophenolate mofetil with high-dose steroids, plus either BENLYSTA or placebo.

Maintenance therapy included azathioprine plus low-dose steroids for those patients who received cyclophosphamide at induction, or mycophenolate mofetil plus low-dose steroids, plus either BENLYSTA or placebo.

BENLYSTA 10 milligrams per kilogram or placebo was administered by I.V. infusion on days 0, 14, and 28, and at 4-week intervals thereafter through week 104.

Treatment failure was defined as patients taking a protocol-prohibited or restricted medication including corticosteroids above 10 milligrams per day for treatment of a renal event after week 24.

An aspect of BLISS-LN is that BENLYSTA was studied as add-on to mycophenolate mofetil or cyclophosphamide during both the induction and maintenance phases of treatment.

The primary endpoint in this trial was renal response, which was measured at week 104. Renal response was defined as eGFR greater than or equal to 60 milliliters per minute per 1.73 meters squared, or eGFR no worse than 20% below pre-flare value, UPCR less than or equal to 0.7, and not a treatment failure at week 104. Significantly more BENLYSTA patients achieved renal response versus placebo,

43% versus 32%, respectively.

Dr. Doghramji:
Now, let's dig into that data further. Can you tell us about the secondary endpoint, complete renal response?

Dr. Caster:
Complete renal response, or CRR, at week 104, was defined as eGFR greater than or equal to 90 milliliters per minute per 1.73 meters squared, or eGFR no worse than 10% below the pre-flare value, and UPCR less than 0.5, and not a treatment failure.

Significantly more patients treated with BENLYSTA achieved complete renal response at week 104, with 30% of patients on BENLYSTA achieving CRR, while only 20% of patients on placebo achieved the endpoint at week 104.

For patients on BENLYSTA, this translates to 74% greater odds of achieving a CRR at week 104 compared with those who received placebo.

Dr. Doghramji:
Now, what was the impact on kidney function for these patients?

Dr. Caster:
In a post hoc analysis, kidney function was assessed using two endpoints.

First, we have the percentage of patients experiencing one or more renal flare between weeks 24 and 104. During this time, 26% of patients on placebo had at least one flare, while only 14% of patients on BENLYSTA had at least one flare.

This descriptive analysis represents a 55% reduced risk in renal flares for the patients treated with BENLSYTA.

Dr. Doghramji:
Doctor, why is reduction of renal flares important for patients with lupus nephritis?

Dr. Caster:
Remember, that as the number of flares accumulates, potential nephron loss increases, and kidney function is compromised, increasing the risk of end-stage kidney disease.

The other post hoc endpoint used to assess kidney function is the eGFR slope. This endpoint is defined as a change in eGFR from week 24 to week 104. For patients on placebo, the slope was a decline of 5.72 millimeters per minute per 1.73 meters squared per year, indicating eGFR loss. For patients on BENLYSTA, the slope was a decline of 2.12. The difference in the two slopes is 3.61, representing 63% less eGFR loss over time for patients treated with BENLYSTA.

Dr. Doghramji:
Now, we also hear about steroid burden in patients with lupus nephritis. Did BENLYSTA help patients reduce their steroid doses?

Dr. Caster:
As we reviewed in the study design, the trial included a mandatory steroid taper to 10 milligrams per day or less by week 24.

Additionally, 41% of patients treated with BENLYSTA reduced their steroid dose to 7.5 milligrams per day or less at week 104, as compared to only 30% of patients treated with placebo. These results are descriptive.

Steroid sparing was another efficacy endpoint in BLISS-LN. The percentage of patients reducing their steroid dose to less than or equal to 7.5 milligrams per day at week 24 was 22% for both BENLYSTA and placebo.

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. Doghramji:
Can you speak to the urgency around treating lupus nephritis? How can we help minimize the kidney damage we've touched on throughout this discussion?

Dr. Caster:
As we discussed at the beginning of our conversation, renal flares and the progression to end-stage kidney disease are the main concerns. So controlling the flares and controlling the disease activity are ways to help minimize kidney damage.

ReachMD Announcer:
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.

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. Doghramji:
Finally, I want to thank my guest, Dr. Dawn Caster, for discussing the burden of lupus nephritis and sharing her insights on the clinical data for BLISS-LN.

Dr. Caster, it was great speaking with you today.

Dr. Caster:
Thank you for having me.

ReachMD Announcer:
This program was sponsored by GSK. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature. This is ReachMD. Be Part of the Knowledge.

References:

1. Almaani S, Meara A, Rovin BH. Update on Lupus Nephritis. *Clin J Am Soc Nephrol*. 2017;12(5):825-835.
2. Anders H-J, Saxena R, Zhao M-H, et al. Lupus nephritis. *Nat Rev Dis Primers*. 2020;6(1):7.
3. BENLYSTA [package insert]. Durham, NC: GlaxoSmithKline; 2023.
4. Data on File, GSK.
5. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis*. 2019;78(6):736-745.
6. Furie R, Rovin BH, Houssiau F, et al. Two-year, randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med*. 2020; 383:1117-1128.
7. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res (Hoboken)*. 2012;64(6):797-808.
8. Illei GG, Takada K, Parkin D, et al. Renal flares are common in patients with severe proliferative lupus nephritis treated with pulse

immunosuppressive therapy. *Arthritis Rheum*. 2002;46(4):995-1002.
9. Parikh SV, Rovin BH. Current and Emerging Therapies for Lupus Nephritis. *J Am Soc Nephrol*. 2016;27(10):2929-2939.
10. Rijnink EC, Teng YKO, Wilhelmus S, et al. Clinical and histopathologic characteristics associated with renal outcomes in lupus nephritis. *Clin J Am Soc Nephrol*. 2017;12(5):734-743.
11. Rovin BH, Furie R, Teng YKO, et al. A secondary analysis of the Belimumab International Study in Lupus Nephritis trial examined effects of belimumab on kidney outcomes and preservation of kidney function in patients with lupus nephritis. *Kidney Int*. 2021;S0085-2538(21)00862-0.
12. Sprangers B, Monahan M, Appel GB. Diagnosis and treatment of lupus nephritis flares—an update. *Nature Reviews Nephrology*. 2012;8(12):709-717.
13. Tektonidou MG, Dasgupta A, Ward MM. Risk of end-stage renal disease in patients with lupus nephritis, 1971-2015: a systematic review and Bayesian meta-analysis. *Arthritis Rheumatol*. 2016;68(6):1432-1441.