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Aligning Efficacy With Patient Goals: The Role of SCIg in CIDP Maintenance

Announcer:
Welcome to ReachMD. This medical industry feature, titled “Aligning Efficacy with Patient Goals: The Role of SCIg in CIDP Maintenance,” is sponsored by CSL Behring. Here’s your host, Dr. Jennifer Caudle.

Dr. Caudle:
This is ReachMD, and I’m Dr. Jennifer Caudle. And joining me today to discuss the role of subcutaneous immunoglobulin, therapy in managing chronic inflammatory demyelinating polyneuropathy is Dr. Said Beydoun.

He’s a Professor of Clinical Neurology and the Division Chief of Neuromuscular Medicine in the Department of Neurology at the Keck School of Medicine, University of Southern California, in Los Angeles, California. Dr. Beydoun, welcome to the program.

Dr. Beydoun:
Thanks for having me.

Dr. Caudle:
Of course. Now before we dive in, let’s hear the Indications and Important Safety Information for Hizentra®, Immune Globulin Subcutaneous (Human), 20 percent liquid.

Announcer:
Important Safety Information

Indications and Usage

Hizentra®, Immune Globulin Subcutaneous (Human), 20% Liquid, is indicated for:

• Treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years and older.

• Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to prevent relapse of neuromuscular disability and impairment.

– Limitation of Use: Maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Continued maintenance beyond these periods should be individualized based on patient response and need for continued therapy.

For subcutaneous infusion only.
WARNING: Thrombosis may occur with immune globulin products, including Hizentra. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. For patients at risk of thrombosis, administer Hizentra at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Please stay tuned to hear more Important Safety Information in this program.

Please see full prescribing information for Hizentra including boxed warning at Hizentra.com/HCP

Dr. Caudle:

Let's start with the basics. Chronic inflammatory demyelinating polyneuropathy, or CIDP is a rare, autoimmune peripheral neuropathy resulting in progressive weakness, numbness, and functional impairment in the arms, legs, hands, and feet.[1-3] It's been described as a complex, multifactorial disease.[2,4,5] Can you walk us through what we understand about its underlying pathophysiology?

Dr. Beydoun:
Sure, CIDP is an acquired autoimmune peripheral neuropathy that can present variably in patients it can be progressive, relapsing–remitting, or monophasic. It often leads to significant limitations in physical activity which can really impact quality of life.[6]

So CIDP is postulated to result from an aberrant immune response creating a pro-inflammatory environment, and what makes it complex is that several different immune pathways can be involved.[2,4,5] You've got macrophages and T-cells which contribute to inflammation, autoantibodies that can target nerve antigens, and complement activation which may amplify tissue damage.[2,5,7] All of these pathways can contribute to the demyelination and axonal injury that presents in CIDP.[5,8] So, it's not a single pathway—it's a multi-mechanism pathophysiology. And this is reflected not only in how differently patients can present but also how they respond to treatment.[4,5,8]

Dr. Caudle:
So how does this variability impact treatment decisions for CIDP?

Dr. Beydoun:
Individualizing therapy is such a key part of long-term disease control. And due to the underlying complexity of CIDP pathophysiology, broad-spectrum therapies such as immunoglobulin, or Ig, corticosteroids, and plasma exchange have remained a cornerstone of treatment because they exert simultaneous immunomodulatory activity across a variety of autoimmune mechanisms.[4,5,9]

On the other side of the therapeutic spectrum, we're also seeing interest in more targeted approaches, like FcRn inhibitors. These therapies work by non-selectively reducing circulating IgG, so they can reduce both harmful *and* protective antibodies.[10] So while they offer a targeted approach, they may also affect immune balance, which is something to weigh carefully.

Dr. Caudle:
I see. You mentioned that immunoglobulin therapy acts across multiple autoimmune mechanisms in CIDP. I'd love to hear more about that.

Dr. Beydoun:
Well, we don't understand immunoglobulin's full mechanism of action in CIDP, but we do know that it acts through both the Fc Constant Region and the Fab Variable Regions to help inhibit the pathogenic effects of demyelination.[5,11]

- The Fab variable region neutralizes and removes pathologic autoantibodies and reduces pro-inflammatory cytokines and adhesion molecules.[11]
- And the Fc constant region modulates Fc receptors and antagonizes FcRn.[5,11]

Ig also inhibits the complement system and modulates B- and T-cell function.[5,11] The combination of all these mechanisms is believed to reduce inflammatory responses. So immunoglobulin therapy stands out because it acts on multiple fronts to block the mechanisms that drive CIDP pathology.[5,9] And unlike with targeted therapies, immunoglobulin therapy prevents nerve damage from pathogenic autoantibodies while keeping protective antibodies.[5,9]

Patients have options when it comes to how they receive immunoglobulin treatment. It can be given intravenously, often in a hospital or infusion center, or subcutaneously, which can offer the convenience of self-administration in the home.[6] SCIg has been shown to provide similar efficacy to IVIg while offering patients more flexibility in managing their treatment.[6,12] And Hizentra was the first approved SCIg for CIDP with an established efficacy and safety profile.[6,13]

Dr. Caudle:
So what does the European Academy of Neurology and Peripheral Nerves Society, or EAN and PNS, clinical guideline recommend in terms of immunoglobulin therapy in managing CIDP?

Dr. Beydoun:
Well, intravenous Ig, or IVIg, is one of the first-line treatment options that's strongly recommended by the EAN and PNS guideline for CIDP.[3] And that really reinforces the central role of broad-spectrum immunomodulatory therapies in this disease. Then for maintenance

Fab=Fragment antigen-binding, Fc=Fragment crystallizable, FcRn=Neonatal Fc receptor

treatment, the guideline also strongly recommends SCIg, such as Hizentra, for patients who've responded to IVIg.[3]

The guideline notes practical benefits to SCIg, like the potential for self-administration at home and possibly fewer systemic side effects compared to IVIg, which can be valuable for patients seeking more independence or who've had tolerability concerns.[3] Now that being said, the EAN and PNS guideline does not express a preference in IVIg versus SCIg for maintenance treatment but it emphasizes that treatment should be tailored for the individual—based on response, patient needs, and shared decision-making.[3]

Dr. Caudle:
With all this in mind, what changes, if any, are you seeing in approaches to CIDP management?

Dr. Beydoun:
That's a timely question because I've seen a shift toward more personalized care for CIDP maintenance therapy given the variability in underlying mechanisms, patient presentation, and response to therapy. CIDP is chronic but can be unpredictable, so once controlled, the focus is toward achieving long-term stability, preserving function, and giving patients more autonomy in how they manage their treatment.

SCIg is part of this shift. And as clinicians increasingly engage patients in shared decision-making, SCIg offers an option that may align with patient priorities and preferences.[3]

Dr. Caudle:
For those just tuning in, you're listening to ReachMD. I'm Dr. Jennifer Caudle, and today I'm speaking with Dr. Said Beydoun about the role of Hizentra, Immune Globulin Subcutaneous Human, 20 percent liquid.

Now this brings us to the evidence. What does the clinical data tell us about Hizentra's efficacy and safety in CIDP?

Dr. Beydoun:
The 24-week double-blind, placebo-controlled phase three study, the PATH study, enrolled 172 CIDP patients who had responded to IVIg and were clinically stable. They were then switched to weekly Hizentra at either 0.2 or 0.4 grams per kilogram per week, or to placebo.[14]

Here's what the study showed[6]:

- Only 36.8 percent of patients in the placebo group did not experience relapse or withdrawal
- But Hizentra prevented relapse or withdrawal in 61.4 percent of patients in the low-dose group.
- And in 67.2 percent of patients in the Hizentra high-dose group

That's an absolute risk reduction of up to 30 percent with Hizentra versus placebo.[6] And in fact, most patients in the PATH study remained relapse-free over the follow-up period. In a pre-specified sensitivity analysis, all patients who withdrew from the study for reasons other than relapse were assumed not to have had a relapse. The proportion of patients who remained relapse-free at 24 weeks were 81 percent in the high-dose group and 67 percent in the low-dose group, versus 44 percent in the placebo group.[6]

A similar trend was observed in the 48-week PATH open-label, extension study, which enrolled 82 patients. Here, 90 percent of patients in the high-dose group and 52 percent of patients in the low-dose group remained relapse-free.[13] And patients across both doses maintained function based on measures like INCAT, I-RODS, grip strength, and MRC scale.[6,13]

Dr. Caudle:
Thank you for walking through the efficacy data. And to follow-up, what can you tell us about the safety profile of Hizentra from the PATH studies?

Dr. Beydoun:
The PATH studies—where patients switched from IVIg to SCIg— also looked closely at safety.[6,13] Local reactions were the most common side effects seen with Hizentra. About 94.5 percent of local reactions were mild, with 5.5 percent moderate, and none were severe. The frequency of local reactions tended to decrease over time.[6,13,15]

There were also systemic adverse events, which were generally mild to moderate.[6,13] Among systemic events occurring in five percent or more of patients, we saw things like headache, fatigue, nasopharyngitis, upper respiratory infections, arthralgia, pain, and fall. Serious adverse events were rare, and only one—an acute allergic skin reaction—was considered related to treatment.[6,13]

And from more than 4,200 recorded SCIg infusions, the data shows that over 93 percent had no reported adverse events. Also, the

INCAT=Inflammatory Neuropathy Cause and Treatment Scale; I-RODS=Inflammatory Rasch-built Overall Disability Scale; MRC Scale=Medical Research Council Scale

systemic adverse event rate from these infusions was 3.6 times lower than the rate of systemic adverse events reported during the 956 IVIg infusions during the open-label restabilization phase of the PATH study. This difference should be interpreted with caution as there was no parallel group of subjects receiving placebo in the restabilization phase.[6] So overall, the safety profile was consistent with what we'd expect from SCIg.

Dr. Caudle:
That's helpful perspective on the safety side. And to build on that, are there other characteristics of SCIg that differ from IVIg?

Dr. Beydoun:
Yes—a major difference is how Ig levels are maintained over time. IVIg is necessary at the start of the treatment to help patients regain function and disease stability, but its less frequent dosing can lead to extreme peaks and troughs in Ig levels. These peaks can put patients at risk for systemic side effects, and the troughs can sometimes allow for CIDP symptoms to return just before the next infusion.[1,3,12,16]

SCIg offers a smoother pharmacokinetic profile. Because it's dosed more frequently in smaller amounts, it helps maintain stable Ig levels, which may reduce the potential for CIDP symptom return between infusions.[12]

There's also the administration itself. After receiving training from their healthcare provider, patients can self-infuse SCIg at home, which may avoid the hassle of scheduling time and traveling to an infusion clinic. And since Hizentra is administered subcutaneously, it avoids venous access challenges often associated with IVIg. And Hizentra is available in ready-to-use pre-filled syringes, which can also ease self-administration for patients.[6]

Dr. Caudle:
As we wrap up, what are some key considerations from our discussion today for clinicians who manage long-term CIDP care?

Dr. Beydoun:
We're seeing a shift toward flexible, patient-centered models that focus not just on symptom control, but on long-term function and stability.

One key consideration in choosing therapies that align with both the clinical picture and the patient's goals. So for some, that may mean switching to SCIg, which is recommended in the EAN and PNS guideline as a maintenance option for adult patients who've responded to IVIg.[3] And in such cases, Hizentra may be an appropriate treatment option.

Data from the PATH and PATH extension studies also support its role in sustaining disease control over time.[6,13] The transition is straightforward, Hizentra should be initiated one week after the last IVIg infusion. And when it comes to dosing, Hizentra is available in two different dosing regimens – 0.2 or 0.4 grams per kilogram per week. Ultimately, it's about matching the treatment to the patient—through shared decision-making and a personalized approach to long-term care.

Dr. Caudle:
Well, thank you for those final comments bring us to the end of today's program, I want to thank my guest, Dr. Said Beydoun, for his insights on the role of Hizentra, a SubQ IG, in the management of CIDP.

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

Dr. Beydoun:
Thanks for having me.

Dr. Caudle:
And for ReachMD, I'm your host Dr. Jennifer Caudle.

Please stay tuned to hear some Important Safety Information.

Announcer:
Hizentra is contraindicated in patients with a history of anaphylactic or severe systemic reaction to human immune globulin (Ig) or components of Hizentra (eg, polysorbate 80), as well as in patients with immunoglobulin A deficiency with antibodies against IgA and a history of hypersensitivity. Because Hizentra contains L-proline as stabilizer, use in patients with hyperprolinemia is contraindicated. IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions. Thrombosis may occur following treatment with Ig products, including Hizentra.

Monitor patients for aseptic meningitis syndrome (AMS), which may occur following treatment with Ig products, including Hizentra. In

patients at risk of acute renal failure, monitor renal function, including blood urea nitrogen, serum creatinine and urine output. In addition, monitor patients for clinical signs of hemolysis or pulmonary adverse reactions (eg, transfusion-related acute lung injury [TRALI].

Hizentra is derived from human blood. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD agent and its variant (vCJD, cannot be completely eliminated.

The most common adverse reactions (observed in ≥5% of study subjects were local infusion-site reactions, as well as headache, diarrhea, fatigue, back pain, nausea, extremity pain, cough, upper respiratory tract infection, rash, pruritus, vomiting, upper abdominal pain, migraine, arthralgia, pain, fall, and nasopharyngitis.

The passive transfer of antibodies can interfere with response to live virus vaccines and lead to misinterpretation of serologic test results.

Please see full prescribing information for Hizentra [at HIZ.COM], including boxed warning.

To report SUSPECTED ADVERSE REACTIONS, contact the CSL Behring Pharmacovigilance Department at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

This medical industry feature was sponsored by CSL Behring. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can Be Part of the Knowledge.

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