Transcript Details

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Exploring Early Usage of a 2L ITP Treatment Option: Clinical Profile and Access Resources

Announcer:

You're listening to *Project Oncology* on ReachMD. This medical industry feature, titled "Exploring Early Usage of a 2L ITP, Immune Thrombocytopenia, Treatment Option: Clinical Profile and Access Resources," is sponsored by Amgen.

Here's your host, Dr. Charles Turck.

Dr. Turck:

Welcome to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and today, we'll review the clinical trial efficacy, safety, and access data for second-line therapy with romiplostim, or Nplate®, in adult patients with immune thrombocytopenia, or ITP for short. Joining me in this discussion is Dr. Steven Fein, who's the founder of Heme On Call, a telemedicine-based benign hematology practice. Dr. Fein, welcome to the program.

Dr. Fein:

It's a pleasure to be here!

Dr. Turck:

Before we dive in, let's take a moment to learn about the Indication and some Important Safety Information for Nplate®.

Announcer:

INDICATION

Nplate® is a thrombopoietin receptor agonist indicated for the treatment of thrombocytopenia in adult patients with immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Nplate® is not indicated for the treatment of thrombocytopenia due to myelodysplastic syndrome (MDS) or any cause of thrombocytopenia other than ITP. Nplate® should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increase the risk for bleeding. Nplate® should not be used in an attempt to normalize platelet counts.

IMPORTANT SAFETY INFORMATION

Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia

- In Nplate® (romiplostim) clinical trials of patients with myelodysplastic syndromes (MDS) and severe thrombocytopenia, progression from MDS to acute myelogenous leukemia (AML) has been observed.
- Nplate® is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than ITP.

Please see additional Important Safety Information for Nplate® in this presentation and at Nplatehcp.com.

Dr. Turck:

Now that we've heard that Important Safety Information, let's begin by considering our adult patients with ITP who require second-line treatment. Dr. Fein, what do the current treatment guidelines recommend?

Dr. Fein:

The American Society of Hematology, or ASH, guidelines state that steroid use of six weeks or less is preferred in adults versus prolonged continuous use.[1]

And the International Consensus Report, or ICR, recommends six weeks or a maximum of eight weeks of steroid treatment in adults who achieve a response.[2]

Unfortunately, most adult patients who complete their initial treatment with steroids end up with their platelet counts dropping again and will need a second-line treatment option.[2]

And so the ASH guidelines suggest a thrombopoietin receptor agonist, or TPO-RA, such as Nplate® as a second-line therapy over rituximab, which is not FDA-approved for use in ITP.[1,3]

Actually, Nplate® has been studied across all stages of ITP in adults. But I'd like to point out that clinical trial data supports Nplate® earlier usage right after insufficient response to steroids with the goals of achieving a quick response with platelet stability and opportunity of treatment-free remission.[4,5]

Dr. Turck:

I'd like you to walk us through those data in a moment, but first, could you describe the clinical trial design for adults with newly diagnosed and persistent ITP?

Dr. Fein:

I'd be happy to. The basis of this study was the clinical observation that some patients retained a response after being on Nplate® for some time, despite missing a dose.[4]

And so Nplate® was studied in a 52-week, open-label, single-arm, phase-two trial in 75 adults with ITP.[4,5] The trial included adults diagnosed with ITP in the previous six months who had an insufficient response to first-line treatment, which included corticosteroids, immunoglobulins, anti-D immunoglobulin, or vinca alkaloids.[4,5] All in all, 96 percent of patients had received prior corticosteroid treatment.[4]

Now it's important to keep in mind that all patients in this trial started treatment with Nplate® early on as their *first* second-line therapy.[4] Patients received Nplate® within a median of 2.2 months from diagnosis, ranging from three days to 6.6 months.[5]

The primary endpoint of the trial was the cumulative number of months in which a patient achieved a median platelet count of at least 50,000.[4]

And the secondary endpoint was the rate of remission, which was defined as maintaining every platelet count at a minimum of 50,000 for at least six months without any ITP treatment.[4]

In order to achieve platelet stabilization, all patients on the study started Nplate® at one microgram per kilogram and then had the dose adjusted weekly until they achieved a platelet count of 50,000 to 200,000.[4,6] Dose adjustments were made following the recommended dosage regimen in the Nplate® prescribing information.[5]

And then, to study treatment-free remission, the trial was designed to either taper patients off of Nplate® after the 12-month treatment period or reduce the dose earlier for patients whose platelet count reached a certain level.[4]

Patients with platelet counts over 200,000 and less than 400,000 for two consecutive weeks had their dosage tapered down by one microgram per kilogram until they were stabilized under this threshold.[4,6]

And at the end of the study period, patients whose platelet count was at least 50,000 had their dose similarly reduced until they were below this threshold.[4,5]

Dr. Turck:

Now with that background in mind, let's dive into the data. Dr. Fein, how about we start with the efficacy results?

Dr. Fein:

Yes, let's take a closer look. A platelet response was defined as a platelet count of at least 50,000 during the 12-month treatment period, which 93 percent of study patients achieved on Nplate®.[5]

Notably, platelet response had a rapid onset, as early as seven days, with a median time to onset of 2.1 weeks.[5,7] And we also see lasting stability of the platelet response, with 61 percent of patients sustaining platelet counts of at least 50,000 for 11 months or more.[4]

Second-line treatment with Nplate®, when administered early in the disease course, also provides patients the opportunity for treatment-free remission. In this study, 32 percent of patients achieved remission without needing any ITP treatment.[4,5]

In the 24 out of 75 study patients who achieved remission, the median time to onset was 27 weeks—meaning nearly half of the patients were on Nplate® for about six to seven months prior to entering the treatment-free remission.[5]

So what we've seen with this phase two trial is that with early use of second-line Nplate®, as early as right after an insufficient response to first-line steroids, patients can achieve rapid onset of lasting platelet stability and can potentially achieve treatment-free remission without needing any ITP therapy.[4]

Dr. Turck:

Now you just mentioned the treatment-free remission results of this phase two trial, and before we move on to review the safety profile, I'd like to hear more about this opportunity for remission in patients with ITP. What can you tell us?

Dr. Fein:

I'm really glad you asked about this, because in addition to this phase two trial, Nplate® has also been studied in an observational, retrospective, real-world evidence study. As you will see, the results of this study supports why it might be important to choose Nplate® at second line.[8]

This multicenter study of 121 adults with ITP up to 5.6 years after diagnosis was made up of approximately 20 newly diagnosed, 19 persistent, and 82 chronic ITP patients. It wasn't powered or designed to assess efficacy of the treatment groups.[8]

Here, therapy-free response was defined similarly to treatment-free remission from the clinical trial we reviewed, requiring maintenance of platelet counts of at least 50,000 for at least six months without any ITP treatment.[8]

And in this real-world evidence study, 51 percent of patients who started and remained on Nplate® in second-line achieved treatment-free remission AND eight percent of patients who started Nplate® achieved treatment-free remission in third-line.[8]

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Dr. Turck:

For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Steven Fein about the efficacy and safety data that support Nplate® as the initial second-line treatment for adults with ITP.

So now that we've reviewed the results of this real-world evidence study, let's return to the phase two clinical trial we looked at earlier. Dr. Fein, how about we turn to the safety findings from this study?

Dr. Fein:

Sure. So overall, Nplate®'s safety profile from this study was consistent with its known safety profile, with no new safety signals observed.[4] This is also consistent with long-term safety data from up to five years of continuous Nplate® treatment.[9]

The most common adverse events during the treatment period, in descending order of frequency, were: headache, arthralgia, nasopharyngitis, hematoma, and cough. The most common bleeding events were hematoma, petechiae, and epistaxis, with no serious bleeding reported.[4]

Serious treatment-related adverse reactions were reported in one patient each for gastritis, reversible ischemic neurologic deficit, and increased transaminases—the latter also led to Nplate® discontinuation.[4]

And keep in mind that Nplate® has been used by a total of almost 500,000 patients over the 15 years that it has been on the market.[5,10,11]

Dr. Turck:

Thanks for sharing those key findings, Dr. Fein. And now, let's listen to some more Important Safety Information for Nplate®.

Announcer:

Important Safety Information, continued

Thrombotic/Thromboembolic Complications

- Thrombotic/thromboembolic complications may result from increases in platelet counts with Nplate® use. Portal vein thrombosis has been reported in patients with chronic liver disease receiving Nplate®.
- To minimize the risk for thrombotic/thromboembolic complications, do not use Nplate® in an attempt to normalize platelet counts. Follow the dose adjustment guidelines to achieve and maintain a platelet count of ≥ 50 x 10^9/L.

Please see additional Important Safety Information for Nplate® in this presentation and at Nplatehcp.com.

Dr. Turck:

Now that we've heard this Important Safety Information, I'd like to shift gears a bit and touch upon Nplate® dosing. Can you provide some insight into dosing and titration for the best chance to achieve results similar to the trial?

Dr. Fein:

Absolutely. Nplate® is a weekly in-office subcutaneous injection that doesn't require liver monitoring or dietary restrictions, and it has no known drug interactions.[5,12,13]

For your best chance of achieving results comparable to the clinical trial, dose and titrate Nplate® as indicated on its label.[4,5]

Nplate® is started at a dose of one microgram per kilogram based on actual body weight, and then it can be individualized for each patient with up to a maximum weekly dose of 10 micrograms per kilogram.[5]

After the initial dose at week one, the Nplate® dose is adjusted weekly based on platelet count response, so weekly CBCs with platelet counts are required until the dose is stabilized. The goal is to maintain a platelet count between 50,000 and 200,000 for at least four weeks at the same dose.[5]

Once the Nplate® dose is stabilized, we can move to monthly CBCs with platelet counts for maintenance monitoring,[5] just like any other second-line ITP treatment.[14–17]

Dr. Turck:

And now that we have a better understanding of Nplate®'s clinical profiles and dosing titration, what are some next steps for clinicians with patients who are treatment candidates, after the treatment decision has been made?

Dr. Fein:

After the clinical decision has been made, I would like my colleagues to consider that Nplate® is an option for their patients with ITP who have an insufficient response to first-line treatment. In fact, Nplate® has a higher percentage of patients with zero out-of-pocket costs versus oral ITP treatments, at 73 percent versus 56 percent, respectively.[18]

Additionally, 87 percent of commercial and Medicare-insured patients are covered for Nplate® without requiring step-through therapy with other plan-selected treatments.[19]

I've also found in my practice that Amgen support resources helped my patients access Nplate®, and I'd like to share these with my fellow colleagues who might not be aware of them. These resources include Amgen SupportPlus Co-Pay program, which may be able

to help eligible patients who have private or commercial insurance lower their out-of-pocket costs. Amgen SupportPlus also supports patients with its other services, such as the healthcare professional support center, benefits verification assistance, and the Amgen Nurse Partners program.

Dr. Turck:

Lastly, Dr. Fein, what key takeaways would you like to share?

Dr. Fein:

I'd like to start with a call to action for my colleagues, which is to consider Nplate® first for a second-line therapy for patients with ITP who've had an insufficient response to steroids.

As we've reviewed, this is a treatment that offers rapid efficacy that lasts, without known drug interactions or food restrictions, and it's the only ITP therapy that offers treatment-free remission on the label.[4,5]

I'd also like my colleagues to keep in mind that Nplate has an established safety profile, including long-term safety data from up to five years of continuous Nplate® treatment, and 15 years of clinical experience. And since it's a once-weekly, in-office subcutaneous injection, my patients don't need to worry about taking a daily pill.[4,5,9–11,14,16,17]

And for my patients, I keep in mind that Nplate® has broad coverage among commercial and Medicare-insured patients, as well as the highest percentage of patient claims with zero out-of-pocket costs versus oral ITP medications.[18,19]

Dr. Turck:

This has been an excellent discussion, and with those final thoughts in mind, I want to thank my guest, Dr. Steven Fein, for breaking down insights on Nplate® and its key efficacy, safety, and access data supporting its use first in the second-line treatment of ITP.

Dr. Fein, it was a pleasure speaking with you today.

Dr. Fein:

Thanks so much for having me!

Dr. Turck:

For ReachMD, I'm Dr. Charles Turck.

Please stay tuned to hear some Important Safety Information.

Announcer:

Important Safety Information Continued:

Loss of Response to Nplate®

- Hyporesponsiveness or failure to maintain a platelet response with Nplate® should prompt a search for causative factors, including neutralizing antibodies to Nplate®.
- To detect antibody formation, submit blood samples to Amgen (1-800-772-6436). Amgen will assay these samples for antibodies to Nplate® and thrombopoietin (TPO).
- Discontinue Nplate® if the platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the highest weekly dose of 10 mcg/kg.

Adverse Reactions

- In the placebo-controlled trials, headache was the most commonly reported adverse drug reaction, occurring in 35% of patients receiving Nplate® and 32% of patients receiving placebo. Adverse drug reactions with ≥ 5% higher patient incidence in Nplate® versus placebo were Arthralgia (26%, 20%), Dizziness (17%, 0%), Insomnia (16%, 7%), Myalgia (14%, 2%), Pain in Extremity (13%, 5%), Abdominal Pain (11%, 0%), Shoulder Pain (8%, 0%), Dyspepsia (7%, 0%), and Paresthesia (6%, 0%).

- The safety profile of Nplate® was similar across patients, regardless of ITP duration. The following adverse reactions (at least 5% incidence and at least 5% more frequent with Nplate® compared with placebo or standard of care) occurred in Nplate® patients

with ITP duration up to 12 months: bronchitis, sinusitis, vomiting, arthralgia, myalgia, headache, dizziness, diarrhea, upper respiratory tract infection, cough, nausea and oropharyngeal pain. The adverse reaction of thrombocytosis occurred with an incidence of 2% in adults with ITP duration up to 12 months.

Nplate® administration may increase the risk for development or progression of reticulin fiber formation within the bone marrow. This formation may improve upon discontinuation of Nplate®. In a clinical trial, one patient with ITP and hemolytic anemia developed marrow fibrosis with collagen during Nplate® therapy.

Please see additional Important Safety Information for Nplate® in this presentation and at Nplatehcp.com.

Announcer:

This program was sponsored by Amgen. If you missed any part of this discussion or to find others in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge.