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/expert-insights-on-itp-moving-from-first-to-second-line-treatment-options/12466/

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

Expert Insights on ITP: Moving from First to Second-Line Treatment Options

ReachMD Announcer
You're listening to ReachMD. This medical industry feature, titled "Expert Insights on ITP: Moving from First to Second-Line Treatment Options" is sponsored by Amgen.

Here's your host, Dr. Charles Turck.

Dr. Turck:
Immune thrombocytopenia, or ITP, is a blood disorder characterized by low platelets thatcan put the patient at risk for bleeding events[1]. For patients with this condition, platelet counts often fluctuate, and the primary goal of treatment is to get them to stabilize— getting platelet control—and for some adults with ITP, this control can even lead to treatment-free remission, while for others, continued treatment may be appropriate.

This is ReachMD, and I'm Dr. Charles Turck. Joining me to share his insights on ITP treatment selection and use of Nplate® as a second-line option is Dr. Steven Fein. Dr. Fein has been dedicated to helping people with ITP for over two decades. After 15 years as hematologist in hospital-based practice, he established a telemedicine consult service for hematology/oncology, where he now serves as medical director specializing in ITP.

Dr. Fein, welcome to the program.

Dr. Fein:
Pleasure to be with you Dr. Turck.

Dr. Turck:
So, let's just dive right in, Dr. Fein. Steroids have been and continue to be a mainstay of first-line ITP treatment. But in 2019, both ASH and ICR updated their guidelines around ITP treatment so that they now limit the duration of first- line steroids to a maximum of 6 to 8 weeks.[2,3] Can you tell us more about this change?

Dr. Fein:
Yes. So, as you just mentioned, the maximum duration of six to eight weeks of steroids is for patients who respond but become steroid dependent[2,3]. And for those who are steroid-refractory, the recommendation is to wait only up to 2 weeks before moving them onto a second-line treatment option[3]. At that point, they either recommend TPO-RAs, SYK inhibitors, or monoclonal anti CD20 antibodies.

Dr. Turck:
So, this seems like a big shift in practice. What do you think led to it?

Dr. Fein:
Well, there has been research looking at long-term steroid use in patients across several different disease states, and in the case of ITP, both ICR and the ASH panels have concluded that for these patients, the benefits may not outweigh the risks[2,3]. This was the rationale behind the 2019 recommendation for a shorter steroid course, and the guidelines reflect the fact that more treatment options exist today than there were in the past.

Dr. Turck:
And as steroid duration decreases, how can we determine when it's time for patients to move on to a second-line treatment option?

Dr. Fein:
From a clinical perspective, there are two main factors that I take into consideration:

- One is the failure to achieve an appropriate platelet response and control, such that when we give steroids, either platelet counts remain below 30,000, there's a less than 2-fold increase8 in platelets from baseline[3], or the patient has bleeding episodes2.
- The second factor is whether or not there's corticosteroid dependence, which we define as the need for ongoing or repeated steroid therapy for 2 months or more just to maintain platelet counts above 30,000 or to avoid bleeds[2]. Getting to that point of insufficient response is another form of treatment failure in the first-line.

In addition to clinical factors, it's important to keep in mind that the move from first-line to second-line therapies and beyond*has* to be an individualized approach and that patient preference needs to be considered, as outlined in the 2019 guidelines[3].

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Steven Fein about current therapeutic considerations for adult ITP. So, Dr. Fein, now that we have a better sense of your clinical decision- making rationale when moving from first to second-line treatment options, let's talk about those options further and focus on Nplate® in particular. But before we dive in, let's just take a moment to review the indication for Nplate®.

ReachMD Announcer

- 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[4].
- 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[4].

Important Safety Information

- Risk of Progression of Myelodysplastic Syndromes to Acute Myelogenous Leukemia[4]
  - 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[4].
  - Nplate® is not indicated for the treatment of thrombocytopenia due to MDS or any cause of thrombocytopenia other than ITP[4].
  - Additional details on the Important Safety Information for Nplate® will be provided after this discussion.

Dr. Turck:
So, with that important safety information in mind, Dr. Fein, let's zero in on Nplate®. From my understanding, how and when physicians can use Nplate® has changed with the expanded FDA approval that occurred in late 2019. What does that mean for the ITP treatment paradigm?

Dr. Fein:
So first it's important to know that Nplate® has been a familiar treatment for adults with chronic ITP for over 12 years[4]. Now, the definition of chronic ITP is when the patient hits the one-year mark from diagnosis[2]. And with the expanded approval of Nplate®, it's approved for second-line ITP treatment within the first year of diagnosis and can actually be used as an early treatment when the patient is still considered to have persistent ITP[4,5]. That means we can now get ahead and intervene with Nplate® before continuing with the long-term use of steroids.

Dr. Turck:
Now with that being said, Dr. Fein, can you tell us about the trial that led to the FDA approval for the use of Nplate® within the first six months of ITP diagnosis?

Dr. Fein:

Sure. So Nplate® was studied in a 52-week open-label, single-arm, phase 2 trial of 75 adults with newly diagnosed or persistent ITP who've had an insufficient response to first-line treatment, including corticosteroids. 96% of the patients in the trial received prior steroid treatment[4,5,6,7].

The eligibility criteria were based on being diagnosed with ITP within 6 months and showing an insufficient response to first-line treatment, which was defined as platelet counts below or equal to 30,000[4,5]. So this trial was intentionally looking at an earlier population of ITP patients than previous studies, and the median time from diagnosis to receiving Nplate® in the trial was only 2.2 months[4].

Now if we take a look at the endpoints of the trial, the primary endpoint was the cumulative number of months in which a patient achieved a median platelet count at or greater than 50,000[5]. A select secondary endpoint was the rate of remission, which was defined as maintaining every platelet count at or above 50,000 for at least 6 months without any ITP treatment[5].

Dr. Turck:
And what were the results from this Nplate® trial?

Dr. Fein:
In terms of platelet control, 61% of patients achieved a sustained response with platelet counts at or above 50,000 for 11 months or longer during the 12-month treatment period, which met the primary endpoint[5].

And 93% of the patients achieved a platelet response[5] which happened with a median time to platelet response of only 2.1 weeks[4]. Responses actually occurred as early as week 1 of treatment with Nplate®, with the majority of patients responding by week 3[7].

For the first time, we were doing a trial that looked at treatment-free remission with Nplate® in ITP. 24 of the 75 patients achieved treatment-free remission with early Nplate® use, meaning that they maintained their response for at least 6 months after discontinuing Nplate®[4,5].

Dr. Turck:
Thanks for reviewing those results with us, Dr. Fein. Let's switch gears a bit and discuss the safety profile. We know from trials in adults with chronic ITP that most adverse reactions were mild to moderate, with headache being the most commonly reported[10,14]. In this trial, was there anything new or different?

Dr. Fein:
No, the safety profile was consistent with the known profile of Nplate®, and no new safety signals were observed[5].

Dr. Turck:
I see. Now we're almost out of time for today, Dr. Fein, so my last question for you is: How do these trial findings align with your clinical experience, and what potential implications do they have on the second-line treatment of ITP?

Dr. Fein:
Now that we have a better appreciation for the efficacy and safety profile of this TPO receptor agonist medication, we have come to accept that it is a reasonable way to potentially achieve treatment-free remission in some patients. In my experience, patients who are able to come off Nplate® are grateful that they were able to get into treatment-free remission following their second-line treatment.

I've also been able to adjust my ideal patient candidate for Nplate® to now be someone who's early on within the course of their disease and has already received a first-line treatment. And the updated Nplate® indication now allows for patients to have access to Nplate® earlier.

So, by prescribing Nplate® earlier, I might be able to reach my treatment goals for my patients of getting their platelet counts to stabilize and potentially, even achieve treatment free remission.

Dr. Turck:
And with those meaningful insights, I want to thank my guest, Dr. Steven Fein, for sharing his perspectives and treatment considerations in ITP. That brings us to the end of today's program.

Dr. Fein, it was great having you with us today.

Dr. Fein:
Pleasure to be with you Dr. Turck.

Dr. Turck:
And for our listeners, let's take another moment to review some additional important safety information for Nplate®.

ReachMD Announcer

Additional Important Safety Information:

Thrombotic/Thromboembolic Complications[4]

- Thrombotic/thromboembolic complications may result from increases in platelet counts with Nplate® use[4]. Portal vein thrombosis has been reported in patients with chronic liver disease receiving Nplate®[4].
- 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 109/L4.

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®[4].
- 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)[4].
- 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[4].

Adverse Reactions

- In the placebo-controlled trials of adult ITP patients, 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 in adults with a ≥ 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%)[4].
- 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 to12 months[4].
- 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.

This medical industry feature was sponsored by Amgen. If you missed any part of this discussion, visit ReachMD.com/industryfeature. This is ReachMD. Be Part of the Knowledge.

For the full prescribing information and medication guide for Nplate®, please visit the link on the landing page for this episode.

References:

1. Cines DB, McMillan, R. Management of adult idiopathic thrombocytopenic purpura. *Annu RevMed*. 2005;56:425-442.
2. Neunert C, Terrel DR, Arnold DM, et al. American Society of Hematology 2019 guidelines forimmune thrombocytopenia. *Blood Adv*. 2019;3(22):3829-3866.
3. Provan D, Arnold DM, Bussel JB, et al. Updated international consensus report on theinvestigation and management of primary immune thrombocytopenia. *Blood Adv*. 2019;3(22):3780-3817.
4. Nplate® (romiplostim) prescribing information, Amgen.
5. Newland A, Godeau VP, Priego V, et al. Remission and platelet responses with romiplostim inprimary immune thrombocytopenia: final results from a phase 2 study. *Br J Haematol*. 2016;172(2):262-273.

6. Newland A, Godeau B, Priego V, et al. Remission and platelet responses with romiplostim inprimary immune thrombocytopenia: final results from a phase 2 study. *Br J Haematol.* 2016;172(Suppl):1-4.
7. Data on file, Amgen. Time to Onset, biostatistical analysis, 2019.
8. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood.2017;129:2830.