ReachMD Announcer:
Welcome to ReachMD.

This medical industry feature, titled "Helping Protect Patients from Febrile Neutropenia in the Real World", is the first in a series of podcasts sponsored by Amgen. This program is intended for healthcare professionals.

Here's your host, Dr. Charles Turck.

Dr. Turck:
Febrile neutropenia, also known as FN, continues to pose a threat to patients on medium-to-high-risk chemotherapy. Among these patients, FN-related hospitalizations have remained around 200,000[1] each year despite the availability of granulocyte colony stimulating factors, or GCSFs.

This is ReachMD, I'm Dr. Charles Turck, and on today's program we'll get an update on real world evidence that shows how GCSF delivery with Neulasta® Onpro® can make a clinical difference.

Neulasta® is indicated to decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.[2]

Stay tuned for the complete important safety information for Neulasta® later in this podcast. This program is intended for health care professionals only.

Joining me to discuss real-world evidence from a prospective study is Dr. Martin Dietrich. Dr. Dietrich is a medical oncologist with extensive background in medical research, who addresses all aspects of hematologic and oncologic care with a specific focus in the community-based setting. Dr. Dietrich, thanks for being here today.

Dr. Dietrich:
Thank you, Charles for having me.

Dr. Turck:
Dr. Dietrich, in your experience, why is it so important to prevent FN, and what is the impact of FN-related hospitalizations on patients, and the cost of care?

Dr. Dietrich:
Well, certainly a few reasons come to mind. In my experience, patients with FN are rarely managed as outpatients, since their FN is considered a medical emergency. The complications from FN that I've observed include delayed clinical care and lower relative dose intensity, as well as decreased performance status and associated increased cost of management of care. In my opinion, it's clearly an important clinical issue that needs to be addressed. For patients receiving high-risk chemotherapy regimens, or regimens with intermediate risk with at least one additional risk factor, we should be using GCSFs up front, to reduce the incidence of FN and associated complications.

Dr. Turck:
With that in mind, let's talk about a GCSF delivery option that can make a clinical difference.

What can you tell us about Neulasta and delivery with the on-body injector, Neulasta® Onpro®?

Dr. Dietrich:
Well, let's start by discussing the data that has convinced many physicians to adopt next-day GCSF therapy.

In the Neulasta® pivotal trial, next-day Neulasta® reduced the incidence of FN by 94%, and reduced FN-related hospitalizations by 93%, compared to placebo.[3]

This study was a Phase 3, multi-centered, multi-national, double blind, placebo-controlled trial of patients with breast cancer, with 463 participants on Neulasta® and 465 on placebo. These participants were receiving 100 milligrams per meter squared, of docetaxel every three weeks, for up to four cycles.[3]

The key endpoint was percentage of patients who developed FN, which was 1% of patients on Neulasta® versus 17% on placebo.

Also, secondary endpoints were lower for Neulasta®- treated patients, as compared to placebo-treated patients. The incidence of hospitalizations was 1% with Neulasta® versus 14% with placebo, and IV anti-infective use was 2% versus 10% with placebo.

Dr. Turck:
Although the results of that pivotal trial may be well known, let's talk about a study designed to reflect what health care professionals may be seeing in the real world.

What can you tell us about the prospective observational study of Neulasta® Onpro®, which was presented as a poster at the 2020 San Antonio Breast Cancer Symposium in December?

Dr. Dietrich:
It's exciting to talk about this first study of its kind. It's unique in that it focused on determining the incidence of FN, adherence and compliance among cancer patients at high or intermediate risk for FN receiving pegfilgrastim with Onpro®, an on-body injector – versus other FN prophylaxis options. In other words, this study investigated the method of GCSF delivery to see if the way a GCSF is delivered makes a clinical difference.

The study enrolled patients from November, 2018 to April, 2020 with a primary analysis that included, 2,575 patients with breast, lung or prostate cancer, or non-Hodgkins lymphoma, who completed up to four cycles of high-FN risk chemotherapy.[4,5]

Patients receiving chemotherapy, with or without curative intent, were categorized into either the Neulasta® Onpro® group or the other FN prophylaxis group, based on the methods received in the first cycle.

Other first cycle treatments included Neulasta® prefilled syringe, biosimilar pegfilgrastim prefilled syringe, daily short-acting filgrastim, or no GCSF.

The primary endpoint was the overall incidence of FN over up to four cycles of chemotherapy.

For patients who received Neulasta® Onpro® in the first cycle, there was a 33% relative decrease in FN versus other FN prophylaxis options. Among people who received Onpro® in all cycles, there was a 36% relative decrease in FN.[4,5]

Dr. Turck:
And how do those results shape your choice of GCSF for your patients, particularly considering the demand for value-based care?

Dr. Dietrich:
There are a number of positive factors that come to mind. When I'm choosing a GCSF, my top priority is to avoid FN and to avoid delays in my patients' chemotherapy schedule.

To reduce the risk of FN for my patients, I choose Neulasta® Onpro®—and these results validate my decision.

In terms of value-based care delivery, these results also lead me to believe I can mitigate the risk of neutropenic fever episodes that, in an untreated setting or in the setting of late recognition, can have substantial implications, both for my patients' outcomes and hospitalization costs, as we discussed earlier.

What I'm also seeing is that the reliable timing of delivery, PEGylated version of GCSF with the Onpro® device, really provides benefits over some of the other daily applications that we would be able to prescribe in the clinic.

In my opinion, these results are telling us, that the way GCSF therapy is delivered does make a clinical difference.

Dr. Turck:
For those just joining us, this is ReachMD.

I'm Dr. Charles Turck, and today I'm speaking with Dr. Martin Dietrich about "Protecting Patients from FN in the Real World."

Dr. Turck:
Dr. Dietrich, tell us more about the real-world evidence from this study with Neulasta® Onpro®.

Dr. Dietrich:
Well, secondary endpoints for this study included adherence and compliance.

Adherence was defined as patients who received G-CSF support for all chemotherapy cycles regardless of timing of G-CSF administration.

Compliance was defined as patients who received pegfilgrastim on the day after the last day of chemotherapy in every cycle in which pegfilgrastim was administered.[5] 94% of patients in the Neulasta Onpro group received GCSF support in all cycles of chemotherapy, compared to 58% of patients in the other FN prophylactic options group.

Dr. Turck:
What do these adherence findings mean to you and the way you treat your patients?

Dr. Dietrich:
Well, it gives me confidence that patients will be getting GCSF support across most or all of their chemotherapy cycles.

The correct timing of GCSF therapy is very important in terms of making sure that each dose is delivered the day after chemotherapy. There is so many logistical challenges that may interfere with a patient's ability to return to clinic on time, and so if I want to be certain that a patient has received pegfilgrastim at the right time as prescribed, I think Onpro® is the logical choice of delivery. When you factor in the challenges that can interfere with next-day delivery from a patient perspective, that compliance drops if that delivery isn't automated.

Dr. Dietrich:
As we saw in the study, more than 95% of patients who received Onpro® received their GCSF at the right time, on the day after the last day of chemotherapy.[5] In my opinion, I think this compliance is as good as it's ever going to be. This compared to 49% of patients who received the pegfilgrastim prefilled syringe or biosimilar pegfilgrastim prefilled syringe. And, as we saw, fewer patients experienced FN with Neulasta® Onpro® vs other FN-prophylaxis options.

This prospective study does have some limitations. First, it was not possible to evaluate FN risk among patients lost to follow-up after study enrollment.

Second, although the analysis of FN incidence, controlled for known baseline differences between the groups, the lack of randomization means that the groups may have differed in ways that were not measured or recorded. The impact of such differences on the study findings are unknown.

And finally, the study closed prematurely due to COVID-19, in the prespecified second interim analysis results. It did not achieve target sample size.

Dr. Turck:
As you mentioned earlier, what are some of the challenges you've seen with patients returning for FN prophylaxis the day after chemotherapy?

Dr. Dietrich:
There are a number of factors to consider. Typically, the patients that I would see felt the worst in the days after chemotherapy, so having to come back to the office simply to get an injection could be cumbersome, and sometimes very difficult to arrange.

Oftentimes, if my patients are taking medications that may be sedating, like nausea medications, they would tell me that it would interfere with their ability to drive independently. There is also the timing of the week to consider. If the patients are being treated on Fridays, they may not be able to get back in time if the offices are closed on Saturdays.

So, there are a number of issues that I have seen, which I believe the automated, next-day delivery with Neulasta® Onpro® is the right choice for my patients.

Dr. Turck:
What final thoughts do you have about Neulasta® Onpro® and the studies we've discussed today?

Dr. Dietrich:
I often tell my patients to maintain your chemotherapy offense, you need to focus on keeping a strong, supportive care defense.

I believe that febrile neutropenia is one of the major risk factors, which is why Onpro® is such an innovation in terms of allowing the patient to receive the full benefit of GCSFs without dealing with some of the inconveniences that are associated with other delivery options.

I think what these studies have uncovered for us is that the logistical challenges in supportive care delivery are very real. They're highly concerning for patients that are not being properly protected against FN. I think we've found a solution to a very pertinent problem, and that solution is to utilize the medication with a more convenient and more reliable method of delivery. And reduction in the risk of febrile neutropenia does have a dramatic clinical impact.

Dr. Turck:
That's a great way to round out our discussion on this topic.

I want to thank my guest for helping us better understand helping protect patients from febrile neutropenia in the real world. Dr. Dietrich, it was great speaking with you today.

Dr. Dietrich:
Thank you so much, it was my pleasure.

Dr. Turck:
I'm Dr. Charles Turck.

Please join us for the next podcast in our Neulasta® series, where we'll discuss results from another real-world study of the impact of Neulasta® on maintaining chemotherapy regimens.

Now, let's review the Important Safety Information for Neulasta®.

ReachMD Announcer:
Important Safety Information:

Contraindication: Neulasta® is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim or filgrastim. Reactions have included anaphylaxis.

Splenic Rupture: Splenic rupture, including fatal cases, can occur following the administration of Neulasta®. Evaluate for an enlarged or ruptured spleen in patients who report left upper abdominal or shoulder pain.

Acute Respiratory Distress Syndrome (ARDS): ARDS has occurred in patients receiving Neulasta®. Evaluate patients who develop a fever and lung infiltrates or respiratory distress after receiving Neulasta®. Discontinue Neulasta® in patients with ARDS.

Serious Allergic Reactions: Serious allergic reactions, including anaphylaxis can occur in patients receiving Neulasta®. Majority of events occurred upon initial exposure and can recur within days after discontinuation of initial anti-allergic treatment. Permanently discontinue Neulasta® in patients with serious allergic reactions.

Allergies to Acrylics: On-body injector (OBI) for Neulasta® uses acrylic adhesives. Patients who are allergic to acrylic adhesives may have a significant reaction.

Use in Patients With Sickle Cell Disorders: In patients with sickle cell trait or disease, severe and sometimes fatal sickle cell crises can occur in patients receiving Neulasta®. Discontinue Neulasta® if sickle cell crisis occurs.

Glomerulonephritis: Has occurred in patients receiving Neulasta®.Diagnoses based on azotemia, hematuria, proteinuria, and renal biopsy**.** Generally, events resolved after dose reduction or discontinuation of Neulasta®. If suspected, evaluate for cause and if cause is likely, consider dose-reduction or interruption of Neulasta®.

Leukocytosis: Increased white blood cell counts of 100 x 10^9/L have been observed**.** Monitoring of complete blood count (CBC) during pegfilgrastim therapy is recommended.

Thrombocytopenia: Thrombocytopenia has been reported in patients receiving pegfilgrastim. Monitor platelet counts.

Capillary Leak Syndrome (CLS): CLS has been reported after G-CSF administration, including Neulasta®.Characterized by hypotension, hypoalbuminemia, edema, and hemoconcentration.Episodes may vary in frequency, severity, and may be life-threatening if treatment is delayed.Patients with symptoms should be closely monitored and receive standard symptomatic treatment, which may include intensive care.

Potential for Tumor Growth Stimulatory Effects on Malignant Cells: G-CSF receptor has been found on tumor cell lines.The possibility that pegfilgrastim acts as a growth factor for any tumor type, including myeloid malignancies and myelodysplasia, diseases for which Neulasta® is not approved, cannot be excluded.

Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) in Patients with Breast and Lung Cancer:MDS and AML have been associated with the use of Neulasta® in conjunction with chemotherapy and/or radiotherapy in patients with breast and lung cancer. Monitor patients for signs and symptoms of MDS/AML in these settings.

Potential Device Failures: Missed or partial doses have been reported in patients receiving pegfilgrastim via the on-body injector (OBI) due to the device not performing as intended.In the event of a missed or partial dose, patients may be at increased risk of events such as neutropenia, febrile neutropenia and/or infection than if the dose had been correctly delivered. Instruct patients to notify their healthcare professional immediately in order to determine the need for a replacement dose if they suspect that the device may not have performed as intended.

Aortitis: Aortitis has been reported in patients receiving Neulasta®. It may occur as early as the first week after start of therapy.Manifestations may include generalized signs and symptoms such as fever, abdominal pain, malaise, back pain, and increased inflammatory markers (e.g., c-reactive protein and white blood cell count).Consider aortitis in patients who develop these signs and symptoms without known etiology. Discontinue Neulasta® if aortitis is suspected.

Nuclear Imaging: Increased hematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient positive bone imaging changes. This should be considered when interpreting bone imaging results.

Most common adverse reactions: Bone pain,Pain in extremity.

Please visit Neulastahcp.com for the Neulasta® full Prescribing Information.

Special Instructions for the On-body Injector (OBI) for Neulasta®: A healthcare provider must fill the on-body injector (OBI) with Neulasta® using the co-packaged prefilled syringe and then apply the OBI to the patient's skin (abdomen or back of arm). The back of the arm may only be used if there is a caregiver available to monitor the status of the OBI. Approximately 27 hours after the OBI is applied to the patient's skin, Neulasta® will be delivered over approximately 45 minutes. A healthcare provider may initiate administration with the OBI on the same day as the administration of cytotoxic chemotherapy, as long as the OBI delivers Neulasta® no less than 24 hours after the administration of cytotoxic chemotherapy.

The prefilled syringe co-packaged in the Neulasta® Onpro® kit contains additional solution to compensate for liquid loss during delivery through the OBI. If this syringe is used for manual subcutaneous injection, the patient will receive an overdose. If the prefilled syringe for manual use is used with the OBI, the patient may receive less than the recommended dose.

Do not use the OBI to deliver any other drug product except the Neulasta® prefilled syringe co-packaged with the OBI. Use of the OBI has not been studied in pediatric patients.

The OBI should be applied to intact, non-irritated skin on the arm or abdomen.

A missed dose could occur due to an OBI failure or leakage. Instruct patients using the OBI to notify their healthcare professional immediately in order to determine the need for a replacement dose of pegfilgrastim if they suspect that the device may not have performed as intended. If the patient misses a dose, a new dose should be administered by single prefilled syringe for manual use as soon as possible after detection.

Review the Patient Information and Patient Instructions for Use with the patient and provide the instructions to the patient

Refer to the Healthcare Provider Instructions for Use for the OBI for full administration information.

For any OBI problems, call Amgen at 1-800-772-6436 or 1-844-MYNEULASTA (1-844-696-3852).

This program—including participation by our guest, Dr. Martin Dietrich—was sponsored by Amgen. If you missed any part of this discussion, visit ReachMD.com/IndustryFeature This is ReachMD. Be Part of the Knowledge.