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/helping-patients-maintain-their-chemotherapy-dosing-schedule/13194/

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Helping Patients Maintain Their Chemotherapy Dosing & Schedule

Announcer:
Welcome to ReachMD.

This medical industry feature, titled “Helping Patients Maintain Their Chemotherapy Dosing and Schedule”, is the second 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 risk to patients on intermediate to high-risk chemotherapy. Each year there are approximately 200,000[1] FN-related hospitalizations despite the availability of granulocyte colony-stimulating factors or G-CSFs. These FN-related events have the potential to disrupt patients’ treatment plans and consequently impact their lives in many ways. To highlight the importance of staying on track with chemotherapy, let’s hear from Bill, a colorectal cancer survivor among the one million patients who’ve been prescribed Neulasta® Onpro®.[2]

Bill:
Neulasta® Onpro® has allowed me to keep up with my chemo plan because I’ve not had to worry about my white blood cell count. It has stayed high enough where I’ve been able to keep going.

Dr. Turck:
For patients like Bill who are at risk of FN, every treatment delay is another chance for cancer to progress. When these patients fall behind in treatment, it may also take more time to administer the full treatment regimen.

As we consider what this means to patients like Bill, today’s program will explore evidence that shows how next-day Neulasta® can help ensure patients stay on track with their treatment plan. This is ReachMD and I’m Dr. Charles Turck.

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.[3] Neulasta® is not indicated for the mobilization of peripheral blood progenitor cells for hematopoietic stem cells transplantation.[3]

Neulasta® is contraindicated in patients with a history of serious allergic reactions to pegfilgrastim or filgrastim. Reactions have included anaphylaxis.[3] Stay tuned for the complete important safety information for Neulasta® later in this podcast. This program is intended for healthcare professionals only.

To discuss the impact that FN may have on patients’ treatment plans, we’re pleased to welcome back Dr. Martin Dietrich. Dr. Dietrich is a medical oncologist with extensive background in medical research who addresses 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:
To start us off, Dr. Dietrich, what are the most important things you take into consideration when formulating a patient's treatment plan?

Dr. Dietrich:
There's so many factors that can increase a patient's risk of FN and so many complications that can result from FN during treatment. I always think about how those complications may compromise the patient's ability to stay on track with their treatment.

Dr. Dietrich:
That's why I follow the NCCN guidelines that suggest considering Neulasta® or Neulasta® Onpro® for patients receiving high-risk chemotherapy regimens or regimens with intermediate risk and one or more risk factors for FN.[4] For example, if I have a patient that is older that may have been pre-treated that may have a diminished glomerular reserve or other risk factors that may be contributing to a heightened risk of infection or bone marrow compromise, I think those are additional factors that I would take into consideration here, as well.

Dr. Turck:
Thanks for that perspective, Dr. Dietrich. What happens when one of your patients misses a dose of G-CSF and then calls back with a fever. How does this impact your patient's treatment schedule?

Dr. Dietrich:
Well, febrile neutropenia can be very disruptive to a patient's treatment and treatment strategy.[5] In my experience, FN complications can include delayed clinical care, delayed chemotherapy, and certainly an increase of cost of care for their management.

Dr. Turck:
Well, with that in mind, let's talk about how G-CSF therapy with next-day Neulasta® can help patients stay on their treatment plan. What should our listeners know about Neulasta®?

Dr. Dietrich:
Well, let's start by discussing the data that has influenced the decision of many physicians to adopt next-day Neulasta®. The Neulasta® study was a phase 3, multi-centered, multi-national, double-blind, and placebo-controlled trial of patients with breast cancer with 463 participants on Neulasta® and 465 on placebo. These participants were receiving 100 mg/m^2 of docetaxel every three weeks for up to four cycles.[6] In this trial, next-day Neulasta® reduced the incidence of FN by 94% and reduced FN-related hospitalizations by 93%, compared to placebo when used every cycle.[6] This study demonstrated that Neulasta® administered on the day after chemotherapy in every cycle significantly reduced the incidence of FN and it highlighted the importance of next-day G-CSF delivery.

Dr. Turck:
Thanks for that background, Dr. Dietrich. Those results helped to show the significance of administering Neulasta® the day after chemo, which sets the scene nicely for the rest of our discussion.

Let's continue by discussing a different kind of study; a real-world retrospective study focused on how next-day Neulasta® delivery helps maintain your patients' treatment plans.[7] Dr. Dietrich, what were the objectives of this study?

Dr. Dietrich:
The objective of this real-world retrospective study was to explore the ability of next-day Neulasta® to help patients receive their planned chemotherapy dosing and schedule. It quantified the association between next-day Neulasta® and relative dose intensity, which is often referred to as RDI.[7]

Dr. Turck:
Can you briefly explain for our listeners how you define RDI?

Dr. Dietrich:
Sure. I'd be happy to do so. Dose intensity is defined as the delivered dose of chemotherapy per unit of time. Relative dose intensity, or RDI, is expressed as a percentage calculated as the delivered dose intensity divided by the standard dose intensity. In other words, RDI

is the extent to which a patient receives treatment according to their treatment plan. So, low RDI may be indicative of more chemotherapy dose delays and more dose reductions, which may disrupt the patient's ability to maintain their treatment plan and obtain optimal outcomes.[5]

Dr. Turck:
Thanks for that clear explanation. Can you briefly describe the study design before we discuss the results?

Dr. Dietrich:
Sure. The study population was comprised of adults undergoing myelosuppressive chemotherapy with high or intermediate risk of FN for primary cancers of the breast, colorectal, lung, or non-Hodgkin's lymphoma.[7] These patients were divided into two groups; one receiving chemo with Neulasta® and the comparator group, which received chemo without G-CSF. The first cycle of each chemotherapy course began with the date of chemo initiation and ended with the first service date for the next administration of chemo for up to eight cycles.[7]

Dr. Turck:
I have some questions about the Neulasta® group. First, did Neulasta® patients receive Onpro® or the pre-filled syringe? Second, did they all receive Neulasta® on the day after chemotherapy?

Dr. Dietrich:
Those are excellent questions, Dr. Turck. The study began before Onpro® became available so the data collection forms were not designed to record the delivery method. Therefore, it wasn't possible to determine whether Neulasta® patients received Onpro® or the pre-filled syringe. However, we do know that the vast majority, about 97% of patients who received Neulasta®, did so on the day after chemo and the analysis limited the Neulasta® group to those patients.

Dr. Turck:
That's helpful background to keep in mind.

Now that we've discussed the study design and objectives, what can you tell us about the results? How did next-day Neulasta® impact RDI?

Dr. Dietrich:
This study showed that next-day Neulasta® helped significantly more patients maintain their RDI. As I mentioned earlier, RDI measures the chemo dose that patients actually received relative to the chemo dose that was planned.[7]

Dr. Turck:
What can you tell our listeners about how maintaining RDI was defined in this study?

Dr. Dietrich:
Another excellent question, Dr. Turck. As commonly reported in the literature, patients with RDI greater than or equal to 85% are considered to have maintained the chemotherapy treatment plan.[5] So, of patients who received next-day Neulasta®, 71% maintained RDI and 29% did not. Among those who were given no G-CSF 55% of patients maintained RDI and 45% did not.[7]

Dr. Turck:
Can you explain for us how the odds ratio was calculated? For simbplicty, walk us through the unadjusted analysis; the one that showed a 98% higher likelihood of maintaining RDI.

Dr. Dietrich:
Absolutely, Dr. Turck. An odds ratio considers two groups and compares their odds of a certain outcome. Specifically for this trial, the outcome was maintaining RDI of greater than or equal to 85%.[7] First, the analysis calculates the odds for each group and then divides one odds by the other to get the odds ratio. For Neulasta®, the odds of maintaining RDI was 71% divided by 29%, yielding an odds of 2.44. For no G-CSF, the odds of maintaining RDI was 55% divided by 45%, yielding an odds of 1.23. Dividing 2.44 by 1.23 gives you the odds ratio, which was 1.98. So, Neulasta® was 98% more likely to maintain RDI than no G-CSF.

Now, we have to keep in mind that this was a retrospective cohort study and not a randomized trial. So, the results could've been

influenced by variables other than Neulasta®, versus no G-CSF; namely baseline clinical and demographic characteristics between the groups. A few notable examples here are age, severity of disease, and type of chemotherapy regimen. To more clearly identify the impact of Neulasta® itself, a follow-up analysis controlled for clinical and demographic differences between the Neulasta® versus G-CSF groups. And as I mentioned earlier, these adjusted results showed that the odds of maintaining RDI was 48% higher with the next-day Neulasta®, which is a statistically significant result as well.

Dr. Turck:
Thanks for the explanation of the results, Dr. Dietrich.

For those just joining us, this is ReachMD. I'm Dr. Charles Turck and today I'm speaking with Dr. Martin Dietrich about how we can reduce the incidence of FN-related events and help patients maintain their chemotherapy schedules.

Let's get back to talking about those patients who already struggle to maintain their chemotherapy schedule.

What could these results mean to you when designing their treatment plan? Would any long-acting G-CSF help you achieve these results?

Dr. Dietrich:
Those are excellent questions. This study tells me that Neulasta® can help patients stay on their treatment plans when it's administered on the day after chemotherapy. I've seen so many logistical challenges that could interfere with the patient's ability to return to the clinic on the day after chemotherapy to receive an injection. That is where the Onpro® device comes in. These results give me a sense of confidence that Neulasta® Onpro® can help my patients stay on their treatment plan because the Onpro® device is specifically designed to deliver Neulasta® at the right time, which is the day after chemotherapy.

Dr. Turck:
What kind of challenges have you run into when trying to ensure that your patients receive a G-CSF injection in the clinic on the day after chemotherapy?

Dr. Dietrich:
Many variables may get in the way of coming back on time for the G-CSF treatment. It could be medically related to how patients are feeling in the days after chemotherapy, especially when it leaves them feeling too weak or sick to travel. Others may have difficulty with the logistical aspect of returning, such as arranging travel, or their own ability to drive themselves back to the office. The patient's own schedule can be a factor, if they have conflict that prevents them from returning or if they receive chemo on a Friday, they may not be able to receive a next-day injection if the offices are closed on Saturdays. So, there are a variety of issues that I've seen, which is why I consistently rely on the automated next-day delivery with Neulasta® Onpro® as the choice for my patients.

Dr. Turck:
With these challenges in mind, I think many patients would agree with your choice.

Let's hear from another one of the million patients who've been prescribed Neulasta® Onpro®. Shaquita is a breast cancer survivor and she had this to say about Onpro® delivery.

Shaquita:
I think the best part about not having to go back to the hospital after chemo is the fact that one, you get the medication that you need through the Neulasta® Onpro®, but it also prevents subjecting yourself to other hospital illnesses, things of that nature. So, for me personally, it's one less time that I need to enter an atmosphere that could potentially subject me or my system to some other type of illness or infection that would cause a delay in my chemotherapy.

Dr. Turck:
With these patients in mind, what are your final thoughts on Neulasta® Onpro® in the studies we've discussed today?

Dr. Dietrich:
As I mentioned in our conversation, I often tell my patients that maintaining their chemotheraphy often starts by keeping a strong

supportive care defense. I believe that febrile neutropenia is one of the major risk factors, which is why I depend on Onpro® to help patients receieve the full benefit of G-CSFs and reduce the potential for interruptions in their treatment plan. I think that Neulasta® Onpro® helps solve a very pertinent problem because it is the medication with the more convenient and more reliable method of delivery.

Dr. Turck: That's a great comment for us to think on as we come to the end of today's program. I want to thank my guest for sharing insights on how to help patients maintain their chemotherapy dosing and schedule in the real world. Dietrich, as always, it was a pleasure to speak with you today.

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Dr. Dietrich:
Well, thank you so much. The pleasure was all mine.

Dr. Turck:
On behlaf of ReachMD, I also want to thank our listener for joining us today. I'm Dr. Charles Turck.

Now, let's review the important safety information for Neulasta®

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 109 /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 GCSF 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 or 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 (for example, 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. Neulasta® is administered by subcutaneous injection. Neulasta® Injection: 6 mg/0.6 mL in a single-dose prefilled syringe for manual use only. Neulasta® Injection: 6 mg/0.6 mL in a single-dose prefilled syringe co-packaged with the on-body injector (OBI) for Neulasta® (Neulasta® Onpro® kit)

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 on 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 the 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.

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