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

Key Considerations for G-CSF Administration in Patients with FN Risk

Announcer:
You're listening to ReachMD. This medical industry feature titled, "Key Considerations for G-CSF Administration in Patients with FN Risk" is sponsored by Amgen.

Here's your host, Dr. Charles Turck.

Dr. Turck:
Febrile neutropenia, or FN for short, is characterized by a low absolute neutrophil count, with fever, and it's a common complication in patients receiving certain types of chemotherapy. Granulocyte colony stimulating factors, or G-CSFs, are agents that are used for primary prophylaxis of FN because they stimulate the bone marrow to produce infection-fighting white blood cells called neutrophils.

This is ReachMD. I'm Dr. Charles Turck, and I'm joined today by Dr. Arielle Heeke to talk about FN risk assessment, guideline recommendations for use of G-CSF in FN prophylaxis, and considerations for G-CSF administration.

Dr. Heeke, thanks for joining us!

Dr. Heeke:
Thank you so much for having me! I look forward to discussing this important topic for treating oncologists.

Dr. Turck:
Now Dr. Heeke, let's dive right into FN risk assessment. What should we keep in mind when assessing this risk, and which patients should be considered for primary prophylaxis with G-CSFs?

Dr. Heeke:
Well the NCCN guidelines recommend assessing febrile neutropenia risk prior to a patient's first cycle of chemotherapy and this risk is based on several factors, including disease, treatment intent, patient risk factors, and the chemotherapy regimen.

In patients receiving chemotherapy regimens that place them at a clinically significant risk for febrile neutropenia, NCCN guidelines recommend granulocyte colony stimulating factor for prophylactic use. When we say clinically significant risk of febrile neutropenia, that means two things: first the patient could be prescribed a high-risk chemotherapy regimen and second the patient could be prescribed an intermediate risk regimen plus one or more patient risk factors for febrile neutropenia.

There are online tools available, such as the febrile neutropenia risk portal that can help assess whether a patient is at high, intermediate, or low febrile neutropenia risk.

Dr. Turck:
Thank you, Dr. Heeke. Can you tell us more about when to administer G-CSFs for FN prophylaxis?

Dr. Heeke:
The historically accepted guidance is to administer growth factor the day after chemotherapy. However, there was a guideline update in May of 2021 which added a statement that there is data for and against G-CSF administration on the same day as chemotherapy.

This strategy is intriguing as patients of course would prefer to receive this therapy on the same day of chemotherapy to minimize trips back to their medical center and during the pandemic this option is even more appealing to minimize infectious exposures in our immunocompromised patients. However, the NCCN guidelines recommend the FDA approved dosing schedule for G-CSFs. The FDA

recommended dosing is that G-CSF be administered on the day after completion of myelosuppressive chemotherapy.

Dr. Turck:
Thank you, Dr. Heeke can you walk us through the data supporting recommended next day administration of G-CSFs?

Dr. Heeke:
Of course. I just want to start by explaining that the current labeling recommendation is to administer growth factor support not sooner than 24 hours after chemotherapy. This allows a neutrophil recovery period and avoids the opposing effects between myelosuppressive chemotherapy and G-CSFs which stimulate neutrophil growth and proliferation. There is a larger more robust body of evidence supporting the use of next day administration. In fact, two types of analyses I'd like to discuss are a systematic review and a meta-analysis, which look at same day vs next day administration of granulocyte colony stimulating factor and particularly echo the benefits of next day administration.

I am aware of one systematic review which included data from 4 randomized control trials, 3 single arm prospective studies, and 7 retrospective studies. The studies included in this review across a variety of tumor types, demonstrated that the administration of G-CSF at least 24 hours after myelosuppressive chemotherapy resulted in improved outcomes. Let's talk a little bit more about the details of these studies. In the randomized studies, the febrile neutropenia rate was higher in cycle 1 when breast cancer patients receive same day vs next administration, with rates of febrile neutropenia of 22% with same day administration vs 7% with next day. This trend was also seen in non-hodgkin lymphoma patients with rates of febrile neutropenia of 11% with same day vs 3% with next day administration. Looking at the retrospective studies, one study included 421 patients with gynecologic malignancies. The majority of patients in this study received next day administration with 332 of those 421 patients receiving next day administration and 89 patients receiving same day administration. Yet, there was higher rate of grade 3 and 4 neutropenia in the same day group and in the next day group. In another large retrospective study that included over 65,000 breast cancer or non-hodgkin lymphoma patients, and across approximately 260,000 chemotherapy cycles, the febrile neutropenia incidence for cycle 1 was 11.4% for same day administration versus 8.4% for the remaining patients. Febrile neutropenia incidence was also higher across all cycles: 7.7% and 6% for same day vs next day, respectively. This study includes by far the most patients of any of prior mentioned references, and it further reinforces the effectiveness of next-day G-CSF administration.

A meta-analysis varies from a systematic review as it is an analysis of a large collection of results from individual studies for the purpose of integrating the findings. The meta-analysis I'd like to discuss includes a relevant database search up to April 2020 and included 1 randomized controlled trail, 11 cohort studies and 1 case-control study. I also chose this study because it adhered to the PRISMA guidelines, which is the gold standard for reporting meta-analyses and systematic reviews. This meta-analysis showed a higher rate of febrile neutropenia in the same-day group compared to next-day. In the first chemotherapy cycle, the odds ratio was 2.56, and across all chemotherapy cycles the odds ratio was 1.54. An odds ratio greater than 1 indicates that the probability of febrile neutropenia was higher for the same day group.

But it's not just higher febrile neutropenia rates we're seeing with same day administration. In two different multicenter, double blind randomized controlled trials, the ANC (Absolute Neutrophil Count) was also observed to be earlier, deeper, and longer in patients with breast cancer or lymphoma compared to next-day administration. This large robust data in support next day administration is indicative as to why it is supported by both clinical guidelines and FDA approved labeling.

Dr. Turck:
For those just tuning in, you're listening to ReachMD, I'm Dr. Charles Turck and today I'm speaking with Dr. Arielle Heeke about granulocyte colony-stimulating factors as primary prophylaxis for febrile neutropenia.

Dr. Heeke, as you mentioned earlier, the guideline update included a statement that there are data in support of same-day administration. Can you share some of those data with us?

Dr. Heeke:
Of course. Well, same day administration is of interest so that the patient doesn't need to return to the clinic after they receive chemotherapy. As a result, there are several studies exploring the safety and efficacy of same day administration. The updated NCCN guidelines cite a single study that may suggest same day administration as an alternative to the recommended next day administration —This was a single-arm, retrospective analysis of 109 colorectal cancer patients, who received G-CSF on the same day as intermediate or high-risk chemotherapy over 4 cycles. The study reported a febrile neutropenia incidence of 3.7% and 4.6% of febrile neutropenia related hospitalizations. This could be considered comparable to rates seen with next day administration.

In addition to this study, there are several other small, retrospective, single institution studies which looked at febrile neutropenia rates and febrile neutropenia-related hospitalizations associated with same day administration, including 3 studies presented at this years

American Society of Clinical Oncology annual meeting. One was a single cohort study of non-hodgkin lymphoma patients receiving a reduced-dose chemotherapy regimen over a series of 100 cycles – with 95 of these cycles completed with same day administration and 5 were next day. Higher incidence of febrile neutropenia and febrile neutropenia-related hospitalizations were observed with same day administration in comparison to next day administration, especially during the first chemotherapy cycle, when patients are at the highest risk for febrile neutropenia. However, this was not statistically significant, which is not horribly surprising considering just 5 cycles were those where patients receive next day administration. In another study of 55 breast cancer patients receiving same day administration, febrile neutropenia incidence and febrile neutropenia-related hospitalizations was observed to be 16.4% and 10.9% respectively. Yet, this study had no comparator arm. And in the 3rd study presented at ASCO looking at same day administration in 114 lung cancer patients, just 1 patient experienced febrile neutropenia and 1 needed to be hospitalized. However, a majority of these patients had a mild risk of febrile neutropenia to begin with.

So to summarize, most of the data for same-day administration are based on small studies with findings that are not statistically reliable. Whereas, next-day administration is based on robust clinical evidence, making it the FDA-approved and NCCN-approved recommendation.

Dr. Turck:
Before we close, Dr. Heeke, do you have any final thoughts you'd like to share with our audience?

Dr. Heeke:
Yes I do, thank you. So G-CSFs are currently approved to be administered approximately 24 hours following myelosuppressive chemotherapy for primary prophylaxis of febrile neutropenia. Although there is ongoing interest in same-day administration, there is certainly more robust data showing that next day administration is associated with improved outcomes.

Dr. Turck:
Very interesting, Dr. Heeke. Well, with those final thoughts in mind, I want to thank Dr. Arielle Heeke for sharing her insights on G-CSF administration for febrile neutropenia risk.

Dr. Heeke:
Thank you! It was a pleasure to be here and to chat with you and your listeners about same day vs next day G-CSF administration.

Announcer
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