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/project-oncology/weighing-the-burden-of-myelosuppression-in-sclc/13585/

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

Weighing the Burden of Myelosuppression in SCLC

Announcer:
You're listening to Project Oncology on ReachMD, and this episode is sponsored by G1 Therapeutics. Here's your host, Dr. Jacob Sands.

Dr. Sands:
Welcome to Project Oncology on ReachMD. I'm Dr. Jacob Sands, and joining me to discuss the burden of chemotherapy-induced myelosuppression in patients with small cell lung cancer is Dr. Jared Weiss, Professor of Medicine in the Division of Oncology in the UNC Lineberger Comprehensive Cancer Center. Dr. Weiss, thank you for joining us today.

Dr. Weiss:
Thank you for having me here today.

Dr. Sands:
So, Dr. Weiss, let's begin by taking a look at the therapeutic landscape for small cell lung cancer. Can you just start out with giving us an overview of the current treatment regimens?

Dr. Weiss:
Sure. So we have basically two stages for small cell lung cancer. Limited stage, meaning that we can encompass it all in a single radiation portal and treat with a goal of cure, and extensive stage, meaning pretty much everything else. Extensive stage small cell lung cancer is one of the cancers more likely to present dramatically, often in the emergency room resulting in admission, because of the central chest syndrome that can occur. Small cell likes to grow in the center of the chest including the lymph nodes, where it can clip off major airways and major vessels, and so response is often very important to us in small cell lung cancer. Fortunately, our treatments do have a very high response rate, albeit limited durability. Our current standard of care, until very recently, evolved not from an improvement in survival, but rather from improvements in toxicity and feasibility. Until very recently, our standard frontline regimen was platinum and etoposide, in the U.S. mostly carboplatin and etoposide. We gave that for two cycles. We got a scan. If it's working, we went to a third and a fourth, and then we watched and waited. More recently, we have two trials looking at PD-L1 inhibitors, that show small but meaningful improvements in survival. And so, our current standard of care is carboplatin and etoposide, plus the PD-L1 inhibitor, atezolizumab or durvalumab, and with that we expect about a year of survival.

Dr. Sands:
Now, the chemotherapy regimens that you've described, certainly can result in hematopoietic stem and progenitor cell damage in the bone marrow. What kind of challenges does this present?

Dr. Weiss:
Well, I think as oncologists, we probably think about neutropenia the most., Febrile neutropenia only happens to a few percent of our patients but it can be a dramatic event and I think when we think about febrile neutropenia, we start either by common sense or with some of the calculators you can find online, calculating a probability of death and considering which patient needs hospitalization, and which patient can be aggressively managed, outpatient with antibiotics and careful monitoring. But that's not the count suppression that's most prevalent. Anemia on an absolute basis is at least as prevalent. And then thrombo – cytopenia very real perhaps about 12 – 12% with carbo/etopo atezolizumab. We don't tend to have a lot of bleeding, but it can result in treatment delays and dose reductions.

The other thing that I think the oncologist doesn't take that seriously, but bothers patients a lot more than it sometimes bothers us, is the incidence of dose delays. So, I think the patient comes in, their counts are a little low, we feel like we're being very humane in delaying

the chemo, we slap each other five, how humane we are. And the patient goes home pretty dejected. This can happen for a number of reasons. Patients can be attached to getting their chemo, and on time, because they accurately perceive it as their lifeline. But also, small cell lung cancer is associated with lower socioeconomic status in the United States. And so what that means, is that the cost of that tank of gas to come in, the cost of parking, the cost of a relative taking that day off of work are a big deal, that we often don't quite properly recognize. And then, of course, the downstream sequelae of these events – febrile neutropenia, of course, can result in death. Anemia results in fatigue, and fatigue is one of the adverse events that we are least equipped to deal with in the office.

Dr. Sands:
So, speaking specifically about that chemotherapy-induced myelosuppression, how prevalent is that in patients with small cell that are undergoing treatment?

Dr. Weiss:
Yeah, it's a great question, because it's far more prevalent than I think a lot of us realize. I think for decades, this has been the cost of doing business with cytotoxic, and so sometimes, something we don't think about it that much. But, in pulling up the toxicity tables of any of the major, Phase 3 trials done recently whether you're talking about carbo/etopo/atezo, carbo/etopo/durva, any of the topotecan trials, any of the lurbinectedin trials – meaning either the randomized Phase 3, or the Phase 1 expansion – what you see is that hematologic events top all of those tables. So thinking about probably the most commonly used regimen in the U.S. – carbo/etopo/atezo – I'm looking as I speak to you, at the toxicity table from EMPOWER 133, the study that led to approval. And in looking at that, I see neutropenia and anemia as the number one and number two events.

Looking at events affecting at least 10 percent of patients, we additionally see decreased neutrophil count, thrombocytopenia, decreased platelet count, leukopenia, decreased white count, and febrile neutropenia all on those top offenders list. And so, it is a big deal, both in terms of things that we traditionally measure, and also the downstream sequelae that our patients feel.

Dr. Sands:
For those of you just tuning in, you're listening to Project Oncology on ReachMD. I'm Dr. Jacob Sands, and today I'm speaking with Dr. Jared Weiss about chemotherapy-induced myelosuppression in patients with small cell lung cancer.

So, Dr. Weiss, you've talked a bit about the prevalence of chemotherapy-induced myelosuppression and some of the burden. Can we talk a little bit more? You've mentioned some of the more impact on quality of life or what the patient would describe, in stating that if you listen during the office visit. Can you dive into that a little bit more? What kinds of things are you listening for, and what are some of the more symptom side effects that these can induce?

Dr. Weiss:
Yeah, it's a really important and a very good question, because no patient comes into the office saying, "Doc, I have myelosuppression. This chemotherapy is terrible." Right? It's not what happens. They may come in saying they have a fever. And we all know about the management of febrile neutropenia, but much, much more often than that is that one of the blood counts is off, such that you need to delay or dose-reduce chemotherapy. Now fortunately, in small cell, we don't have a tight relationship between chemotherapy dose intensity and survival, but if you listen to patients, patients are very much bothered if they can't get their chemotherapy when they expect it. This is their lifeline. And they get nervous when it has to be dose-reduced and particularly when it has to be delayed. In the U.S., there interestingly not as much in western Europe and many other places in the world, but in the U.S., small cell is a disease of largely of underprivileged people. And if you listen to them, the cost of a tank of gas is a big deal, and they have to come back another time. A relative taking off work for the day, to bring them in, is a big deal. And so, I think for oncologists, we say, "ah, we'll wait until next week, no big deal" – and I don't think patients think about it the same way. The other element, of course, of this is cost. The cost of these events is far out of proportion to what common sense might suggest.

Dr. Sands:
And as a quick follow-up to that, of course there is more and more discussion about the cost of care, and such. What kind of impact are you seeing, if at all, to the discussion around some of the myelosuppressive management related to some of the costs that you're describing?

Dr. Weiss:
Well, in the U.S., we don't always talk about cost as much as we perhaps should. Our European colleagues regularly mock us for this, I think rather appropriately. But as we move into models where the oncology practice shares the risk and the potential benefits related to cost management, we're going to be forced to pay more attention to this. And of course, we do pay attention to the costs that our patients perceive, such as having to return for another visit.

Dr. Sands:

So, having discussed the prevalence of chemotherapy-induced myelosuppression and the effect on patients, what are some strategies that we can take to help reduce the burden on patients, and help better manage them, and prevent some of these myelosuppressive events?

Dr. Weiss:
So, traditionally, to reduce chemotherapy-induced myelosuppression, you really had two major options. You could reduce the dose of chemo or give it less frequently, which are really not that different. That's one theme of less chemo. The other thing you could do was to use agents to stimulate the bone marrow to produce additional cells out back. And so the one that we do use in our practice is pegylated filgrastim. This agent does help quite significantly, but it does come with a certain cost, and I don't mean just financial. I mean toxicities of its own, in particular, bone pain, and I think it's a little bit unrecognized in practice how much the discomfort from this agent bothers our patients. And if you listen to our nurses there are logistical problems with it. The new kids on the block, of course, is Trilaciclib, which can proactively pull the bone marrow progenitors out of cycle while the chemo is washing by, in order to preserve them and proactively to preserve blood counts.

Dr. Sands:
Well, with those key strategies in mind, I want to thank my guest, Dr. Jared Weiss, for joining me today to talk about chemotherapy-induced myelosuppression in patients with small cell lung cancer. Dr. Weiss, a pleasure having you on the program.

Dr. Weiss:
Thank you, sir.

Announcer:
This episode of *Project Oncology* was sponsored by G1 Therapeutics. To access this episode and others from this series, visit ReachMD.com/projectoncology, where you can Be Part of the Knowledge. Thanks for listening!