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Sacituzumab Govitecan for mTNBC: A Review of Real-World Efficacy and Safety Data

Announcer:
You're listening to *Project Oncology* on ReachMD, and this episode is sponsored by Gilead Oncology. Here's your host, Dr. Charles Turck.

Dr. Turck:
This is *Project Oncology* on ReachMD, and I'm Dr. Charles Turck. Joining me to discuss a study that examined the real-world effectiveness and tolerability of sacituzumab govitecan in patients with metastatic triple-negative breast cancer is Dr. Paulo Tarantino. Dr. Tarantino is a medical oncologist and advanced research fellow in the Breast Oncology Program at Dana-Farber Cancer Institute and Harvard Medical School. Dr. Tarantino, thanks for being here today.

Dr. Tarantino:
Hello, Charles. Glad to be here.

Dr. Turck:
So why don't we start with some background, Dr. Tarantino. How is sacituzumab govitecan used to treat patients with metastatic triple-negative breast cancer?

Dr. Tarantino:
Sacituzumab govitecan is a Trop2 antibody drug conjugate that basically delivers a highly potent chemotherapy, SN-38, towards tumor cells that express Trop2. And we know that most breast cancers express Trop2, even at high levels. And so it first was approved in 2019 for treating patients with pretreated metastatic triple-negative breast cancer based on very promising phase 1 data that were then replicated and confirmed in the ASCENT trial. And in truth, the drug is currently used for treating patients with metastatic triple-negative breast cancer that received at least one prior line of chemotherapy in the metastatic setting. And based on another phase 3 trial, TROPICS-02, we now use the drug in chemotherapy-refractory patients with hormone receptor-positive metastatic breast cancer as well. So we are starting to use the drug more and more in clinical practice, and usually we use it in patients, once again, with chemo-refractory disease, and this is because all of the trials that were conducted—ASCENT, TROPIC-02, and the phase 1 trials—were in a chemo-refractory population. But now, there is some movement of the drug, and in the future, there is a chance we may be using it even earlier.

Dr. Turck:
Now with that in mind, let's zero in on this new study. What was the goal, and what methods did the study employ?

Dr. Tarantino:
I think whenever there is the approval of a new drug, it's important to understand how the drug performs in our patients in the real world. Of course, patients in clinical trials are enrolled globally, and so you have some patients from the US but also some patients from everywhere else. And also, patients are selected in clinical trials based on inclusion criteria, whereas in the real world, we have many patients that have a performance status that would not make them eligible for trials, organ dysfunction, or other reasons that may make them not exactly like trial patients. So this is why real-world data can really integrate trial data.

And this study that was published by Dr. Kaliski and colleagues really tried to address this: to understand the performance of sacituzumab govitecan in the real world among patients with pretreated metastatic triple-negative breast cancer. And to do so, basically, they looked at the ConcertAI Patient360 platform database, which allowed them to look at the real-world data from 230

patients with triple-negative breast cancer. They included a diverse population that had been previously treated with chemotherapy, so we're talking of second- to third-line patients, quite similar to ASCENT. Although in ASCENT, patients were more pretreated. And they looked both at real-world efficacy outcomes, but also at toxicity outcomes and the use of growth factors. That is also very important.

Dr. Turck:
And is there anything else you can tell us about the patients who were enrolled in this study?

Dr. Tarantino:
This population was diverse, and so there were white patients, but a quarter were Black patients and also Asian patients. Almost 20 percent of the patients had a performance status of 2 or higher, which basically really integrates clinical trial data. Most of the patients—two-thirds—were from the community setting, and so it also integrated the data from academic settings that run clinical trials. The median of prior lines of treatment was 2, and it included both patients with the de novo disease, but also patients with recurrent disease. And once again, these were only patients with triple-negative breast cancer, so trying to mimic the ASCENT trial. And most of the patients, as you would expect in this setting, show metastasis, about three-quarters of the patients. And there even were 7 percent of the patients that had brain metastasis. So in general, a high-risk population that quite nicely mimicked the ASCENT trial.

Dr. Turck:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Charles Turck, and I'm speaking with Dr. Paulo Tarantino about a study on the real-world use of sacituzumab govitecan for metastatic triple-negative breast cancer.

So now that we have a solid understanding of the study's design, Dr. Tarantino, let's turn to the findings. How did sacituzumab govitecan impact patients' overall survival?

Dr. Tarantino:
Yeah, I think there are different metrics of efficacy of the drug in this study, but really, the most important one is overall survival, as you mentioned because it's one that is not biased by so many factors; it's just objective. And in truth, the overall survival observed in this study in pretreated patients with metastatic triple-negative breast cancer was quite promising. There was a median overall survival of 10 months in this population, and about 40 percent of the patients were free from a survival event at 1 year. And there was also a quarter of the population that survived more than 2 years. So, of course, we would hope this metric to be even better, but for a population of patients with the most aggressive subtype of breast cancer— metastatic triple-negative breast cancer—that experience progression on a median of two prior lines, this was quite amazing. And so I do feel that this data quite nicely shows the efficacy of sacituzumab govitecan, leading to nice outcomes or at least better outcomes compared to the past in this population.

Dr. Turck:
And how about its safety? What did we learn about the prevalence and management of adverse events?

Dr. Tarantino:
I have to say, the safety data is, of course, harder to collect in the real world. In truth, what was observed in this study was quite consistent with what we know with this agent. And so we know that it can cause fatigue, which was the most widely reported side effect in this real-world experience. Neutropenia, also. Diarrhea and alopecia. But I'm not sure if I would strongly trust the percentages just because we know that there is underreporting of side effects in the real world. For instance, alopecia was observed in 10-11 percent of the patients, but we know that in truth, the drug causes alopecia in most of the patients. So I think the real-world data are mostly helpful for the efficacy data. But still, it is good to see that the side effects that you commonly see in clinical practice and in trials with sacituzumab govitecan are all reported in this experience.

And one interesting thing is the use of GCSF, which was nicely reported in this trial and in this real-world experience in most of the patients that were treated with sacituzumab govitecan. And we're seeing that there is an increase in uptake and use of growth factors to try to prevent febrile neutropenia. And so in this study, 58 percent of the patients received growth factors with a median only after 8 days. So many patients started early, and probably some of them even extremely early. The earliest administration was 2 days after the start of sacituzumab govitecan. So basically, we're talking of primary prophylaxis here.

And I think we're learning about this day-by-day. There is a curve of learning with every drug, and we are learning that there are some patients that do need primary prophylactic with growth factors because of the risk of neutropenia, especially if they had neutropenia with prior drugs or if they're frail. And so I think this real-world experience is what it shows: that the common toxicities we see in clinical trials are basically observed also, of course, in the real world. There were no unexpected toxicities in the real world with the drug, and growth factors are really being used more and more to prevent severe neutropenia in these patients.

Dr. Turck:

Thanks for breaking down those results for us, Dr. Tarantino. And in our final moments here, what conclusions can we draw from this study, and what do they mean for our clinical practice?

Dr. Tarantino:
I really think that this data reinforces the position of sacituzumab govitecan among patients with chemo-pretreated metastatic triple-negative breast cancer. They basically show that the drug has consistent efficacy, and also—with all the caveats of real-world data—consistent toxicity was observed in clinical trials, reminding us of what an important treatment option it is in patients with chemo-refractory triple-negative breast.

That said, I think in the future, we've got to start using the drug earlier and earlier. Because right now, there are phase 3 trials ongoing with sacituzumab govitecan in the first-line, with or without immunotherapy, for metastatic triple-negative breast cancer. They're called ASCENT-03 and 04. And there are also adjuvant trials ongoing, phase 3 trials. There is the SASHA trial expected to report soon of post-neoadjuvant sacituzumab govitecan. There is OptimICE-RD that is also looking at post-neoadjuvant sacituzumab govitecan with pembrolizumab.

So all of this is moving fast, and I do think we've got to start using this highly effective drug earlier and earlier, and this tells us even more of how important it is to keep collecting real-world data to understand in this evolving scenario how this drug is going to be used, how this drug is going to perform in these novel settings, and what the toxicities are going to be. And what I really hope is that we're going to learn to use this drug better and better. We're going to be able to prevent severe toxicities better and better with prophylactic strategies, and we're going to be able to utilize this drug to get its efficacy while reducing and mitigating the toxicities we see with sacituzumab govitecan and other ADCs as well.

Dr. Turck:
Well, as those final comments bring us to the end of today's program, I want to thank my guest, Dr. Paulo Tarantino, for joining me to share these real-world findings on treating metastatic triple-negative breast cancer. Dr. Tarantino, it was great having you on the program.

Dr. Tarantino:
It was a true pleasure. Thank you so much, Charles.

Announcer:
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