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Advanced Breast Cancer Care: Preventing AEs in Sacituzumab/Govitecan Treatment

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 he presented at the 2024 American Society of Clinical Oncology Annual Meeting that focused on preventing common adverse events associated with sacituzumab/govitecan in patients with triple-negative or HR+/HER2- advanced breast cancer is Dr. Javier Cortes. Not only is he a study author, but he's also the Head of the International Breast Cancer Center in Barcelona and a founding partner of MEDSIR. Dr. Cortes, welcome to the program.

Dr. Cortes:
Thank you very much. It's great to be with you today.

Dr. Turck:
Now if we start with some background, Dr. Cortes, would you tell us about the treatment option sacituzumab/govitecan and its most common adverse events?

Dr. Cortes:
Sure. Well, as you all know, a TROP2 is a surface antigen and it's a membrane receptor, which has been related with cell growth, migration, and invasion, and it is well known that it is highly expressed in breast cancer. So SG, or sacituzumab/govitecan, is the first approved anti-TROP2 antibody drug conjugate, and it has been demonstrated to improve long-term outcomes—both progression-free survival and overall survival—in triple-negative breast cancer and in HR+/HER2- metastatic breast cancer based on the ASCENT and TROPiCS-02 Phase 3 trials, respectively.

So in addition to the efficacy, unfortunately all drugs do have adverse events. As with sacituzumab/govitecan, the most common treatment-emergent adverse events, which has been observed in these Phase 3 trials, were neutropenia and diarrhea. And unfortunately, in some patients, we had to reduce the dose and, in some cases, also interrupt or discontinue the treatment. So based on these two important aspects, we decided to conduct a study called PRIMED to try to decrease these important treatment-emergent adverse events, which were diarrhea and neutropenia.

Dr. Turck:
So now with that in mind, let's zero in on your study. What was the overall objective, and how was it designed?

Dr. Cortes:
So basically, the PRIMED study did have a primary endpoint, which was to evaluate the incidence of neutropenia and diarrhea in patients who received sacituzumab/govitecan in either of these two indications: triple-negative breast cancer or HR+/HER2- metastatic breast cancer. Of note, patients could have received one prior line of chemotherapy in the metastatic disease, but no more than two prior lines of chemotherapy. So in brief, enrolled patients were included from the second- or third-line setting. So in those spaces with HR+ tumors, also patients should have received previous treatment with endocrine treatment and a CDK 4/6 inhibitor.

Patients were treated with sacituzumab/govitecan at the standard dose of 10 milligrams per kilogram on Day 1 and Day 8, every 21-day

cycle, and they also received both drugs, G-CSF and loperamide, during the first 2 cycles. It was administered at a dose of 300 micrograms, two consecutive days, 48 hours after the administration of each of the infusions of sacituzumab/govitecan. And importantly, loperamide was administered during the first 2 cycles, 2 milligrams twice a day or 4 milligrams daily during the first cycle.

Basically, as I said before, the primary endpoint was the incidence of Grade 3 or higher neutropenia and incidence of Grade 2 or higher diarrhea. And for the primary analysis, we wanted to observe that the number of these events were lower, clear lower than expected, without this prophylactic treatment.

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. Javier Cortes about the PRIMED study that examined the prevention of sacituzumab/govitecan-related adverse events in patients with triple-negative or HR+/HER2- advanced breast cancer.

Now if we zero in on the results, Dr. Cortes, what were the key findings concerning the incidence of neutropenia and diarrhea and prophylactic measures against the development of those adverse events?

Dr. Cortes:
Well, a total of 50 patients were included; 32 patients did have triple-negative breast cancer and 18 patients did have HR+/HER2- metastatic breast cancers. According to the key results, during the first two cycles, the incidence of any-grade of neutropenia and diarrhea were 28 and 34 percent, respectively.

Eight patients, 16 percent, did have Grade 3 or higher neutropenia, meeting this primary endpoint with a P-value less than 0.001. Of great interest, no patients developed febrile neutropenia. If we analyze in detail the number of patients with Grade 3 and Grade 4, it was very interesting to know that 6 patients did have Grade 3, 12 percent, and 2 patients did have Grade four, 4 percent.

Regarding diarrhea, 8 patients, 16 percent, experienced Grade 2 or higher diarrhea for a P-value of 0.084. According to the prespecified criteria, we expected to have 7 patients or lower with Grade 2 or higher diarrhea, so this second primary endpoint was not met. However, I think it's very interesting to highlight that in terms of Grade 3, Grade 4, and Grade 2, we had 6, 2, and zero patients, so 12 percent with Grade 2, 4 percent with Grade 3, and zero patients developed Grade 4 diarrhea.

So in my opinion, based on this data, I think that prophylactic treatment with G-CSF clearly achieved the goal we had at the very beginning, and also loperamide decreases, clearly, the number of patients experiencing Grade 2 or higher diarrhea, although it is true that we did not meet the prespecified primary endpoint.

Dr. Turck:
And what did we learn about the impact of these adverse events on dose reductions, treatment interruptions, and medication discontinuation?

Dr. Cortes:
Dose reductions were noted in 14 percent of patients in the PRIMED study compared with 22 percent in ASCENT and 34 percent in TROPiCS-02. Treatment interruptions were 30 percent in our study compared with 61 and 66 percent in ASCENT and TROPICS-02, respectively. And finally, adverse events leading to permanent discontinuations were 0 percent in our study compared with 5 and 6 percent, respectively. It's important to note that we have considered the two first cycles for the primary endpoint, so this trial is still ongoing, and we'll report further data in upcoming meetings.

Dr. Turck:
So given these results, how can we best incorporate prophylactic approaches into clinical practice when treating patients who are receiving sacituzumab/govitecan?

Dr. Cortes:
Well, based on this data, in my opinion, I think that incorporating prophylactic administration of G-CSF is very easy and cheap. So we can do it tomorrow morning if needed. I think this is something that we can incorporate. We know how to manage this as a drug very nicely, and we can clearly decrease the toxicity, dose interruptions, and dose reductions.

Regarding loperamide—although as I said before, the primary endpoint for Grade 2 or higher diarrhea was not met, in my opinion, from a numerical perspective—it was clearly better when the loperamide was added. So in my clinical practice, I have added loperamide at least to the first two cycles, and that's something that I have incorporated in my clinical practice. I would recommend to do it.

Dr. Turck:
And before we close, Dr. Cortes, are there any other key takeaways or final thoughts from your study that you'd like to share with us

today?

Dr. Cortes:
Well, I think that we all know that unfortunately, antibody drug conjugates, although they have changed the way we treat our patients, have adverse events. So if we are able to decrease the toxicity, we might find with these drugs that we will be able to give more doses of these drugs and decrease the possibility of stopping the treatments early. We know that when we decrease the dose or we stop the treatments, this might have important or significant outcome considerations. So in my opinion, if we can administer prophylactic treatments to at least decrease these adverse events, I think that, maybe, we'll be able to optimize long-term outcomes.

Dr. Turck:
Well, with those key takeaways in mind, I want to thank my guest, Dr. Javier Cortes, for joining me to discuss the findings from the Phase 2 PRIMED study and how we can prevent neutropenia and diarrhea in patients with triple-negative or HR+/HER2- advanced breast cancer who are receiving sacituzumab/govitecan. Dr. Cortes, it was great having you on the program.

Dr. Cortes:
Thank you very much for the invitation.

Announcer:
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