Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/expert-panel-integrating-and-optimizing-adcs-in-the-treatment-of-tnbc/14298/

Released: 06/15/2022
Valid until: 06/30/2023
Time needed to complete: 1h 21m

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

Expert Panel: Integrating and Optimizing ADCs In the Treatment of TNBC

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCME curriculum.
Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Bardia:
Welcome to this episode. Today, we'll review "*Integrating and Optimizing Antibody-Drug Conjugates for the Treatment of Triple-Negative Breast Cancer*." Joining me today are Dr. Hurvitz and Dr. Kalinsky. So maybe let's start with sacituzumab govitecan. Dr. Hurvitz, how do you incorporate sacituzumab govitecan in your clinical practice? If you could go through your treatment paradigm and guideline.

Dr. Hurvitz:
Yes. Sacituzumab govitecan showed remarkable efficacy compared to treatment of physician's choice which was single agent chemotherapy. And while the ASCENT study was in the third-line setting and beyond, the approval actually allows for us to use in the second-line setting. And that's my preference, is to use it in the second-line setting after standard chemotherapy, either alone or in combination with pembrolizumab if PD-L1 expression is present. The sacituzumab data certainly did meet the primary endpoint in terms of both progression-free survival and overall survival. And when we're talking about triple-negative breast cancer with so few options available, the fact that this study actually met a survival endpoint is really compelling. Not only for us as clinicians but when I tell patients that it's compelling to them because these are often young women who want to live longer. The side effect profile is something I spend a fair amount of time with, when I'm talking with patients about this therapy. But given the survival benefits most of my patients are highly motivated to do things to help them tolerate the therapy and to go on with this therapy.

Dr. Bardia:
So, regardless of PD-L1 status, whether the tumor is PD-L1 negative or positive, or germline BRCA status, in the second-line setting you would consider sacituzumab govitecan?

Dr. Hurvitz:
Yes, I would. And if they were PD-L1 positive my preference would be to give pembrolizumab in the frontline setting. We know that immune-based therapy works better in the frontline setting than later line settings. So I would choose to to use it there. Often I'll use it in combination with gemcitabine carboplatin, just to allow women to keep their hair. In the second-line setting, if they were someone who carried a germline BRCA mutation, I might be tempted to use a PARP inhibitor in that second-line setting. It would have to be an individualized patient discussion because we do know that PARP inhibitors are better than single-agent chemo in terms of PFS but not yet in terms of OS. So it would be a bit of a discussion how we sequence PARP inhibitors versus sacituzumab govitecan since sacituzumab beat treatment of physician's choice in terms of overall survival. Perhaps the data's a little more compelling there but it's just going to depend on whether the patient's willing to have hair loss and to have IV therapy, etcetera, given the tolerability profile of PARP inhibitors.

Dr. Bardia:

© 2023 ReachMD

That's great. And then, in terms of treating a patient's, Dr. Kalinsky, say you have a patient in front of you, second-line, you're going to prescribe sacituzumab govitecan. What are the things that you usually discuss with the patient in terms of what to expect and side effects?

Dr. Kalinsky:
Yeah, I mean, I also, similar to what Dr. Hurvitz was saying. I also reiterate the overall survival advantage, right? I think that that's really meaningful for all of us. And, you know, the study was halted early because it was all for various endpoints, including survival. The data safety monitoring committee had recommended that the results be reported early. So in terms of the toxicity, you know, we discuss things like nausea and fatigue, alopecia, gastrointestinal issues. I tend to use intravenous antiemetics early and then potentially deescalate if need be, and growth factors when needed. And if patients are experiencing fatigue, I find anecdotally that modification of the dose can be helpful and patients tend to tolerate. And I think that, as Dr. Hurvitz was mentioning, in terms of the time of when to utilize sacituzumab, I have a very similar approach.

Dr. Bardia:
And how about for management of neutropenia? Do you usually start with GCSF or more as secondary prophylaxis, or you prefer dose reduction? What's your practice related to neutropenia?

Dr. Kalinsky:
Yeah, you know, in the study, I believe it was about 50% of patients required growth factor utilization. I don't tend to use it on that first cycle. I tend to utilize it if I'm seeing that patients are experiencing neutropenic issues with the caveat being that there are patients who had previously experienced issues with her counts, then I may have a lower threshold to just start it and kind of see how it goes. But I tend to see how the first cycle goes and then adjust accordingly.

Dr. Bardia:
Makes sense. You can see how the patient is doing and then refine things. That's great. So we covered sacituzumab govitecan extensively in terms of when to use, what to expect, how to educate patients, and then adverse events. So moving on to other antibody-drug conjugates, Dr. Hurvitz, are there other antibody-drug conjugates you're excited about for patients with TNBC?

Dr. Hurvitz:
Well, there was a little study that was presented at ASCO this year, the DESTINY-Breast04 clinical trial, which I think was immediately practice changing in terms of HER2-low expressing metastatic breast cancer. In this study, T-DXd improved PFS and overall survival against treatment of physicians choice. And this study included patients who had hormone receptor-positive breast cancer. We know about two thirds of HR positive breast cancer has low expression of HER2 that doesn't meet overexpression or amplification. And somewhere around a third of patients with triple-negative disease have HER2-low expression. In this study, there was a small subset of patients who had triple-negative breast cancer. I think there were 40 that were evaluable but maybe 60 that were enrolled overall in this study. And it does show a very compelling trend in the right direction in terms of responses, PFS and OS. So I think it's going to be something that we're all focusing on in the future to see if there are biomarkers that can help us select patients that are good candidates for T-DXd that have triple-negative disease. But it also raises a number of questions. How do we sequence this with sacituzumab, where we have very compelling level I evidence from a large phase III trial for all patients with triple-negative disease showing PFS and OS benefits. The two ADCs do have very similar payloads loads that target topoisomerase I. And so we haven't proven one way or another whether using an ADC with a payload that is similar to another one in sequence is actually effective. I think it's really begging us to do clinical trials to test out how we can sequence ADCs that have similar payload mechanisms of action.

Dr. Bardia:
That's a great point. And I guess in the future we'll have to look at ADC sequencing. So, just to continue this conversation, I'll bring this difficult question to Dr. Kalinsky. So if you have a patient with PD-L1 positive TNBC, starts with carbogen pembro first-line and then has disease progression. And the HER2 is low 1+, 2+. And if both drugs are approved sacituzumab govitecan and trastuzumab deruxtecan, what would you use next?

Dr. Kalinsky:
You know, I agree with Dr. Hurvitz's assessment. I think I would utilize sacituzumab govitecan given that we had a dedicated study in triple-negative breast cancer randomized phase III trial. I think that the results with trastuzumab deruxtecan and DESTINY 04 were certainly exciting and compelling. I think you could recognize that just by the response in the room and the co-publication in The New England Journal of Medicine. I do agree that the question about sequencing is going to be increasingly critical. Also, just keeping in mind that, two things: One, sacituzumab govitecan is going to be evaluated in phase III trials in the frontline setting, in a PD-L1 positive and a PD-L1 negative study. So we'll see as this agent continues to move up. And there are other ADCs that are coming down the pike, like Dato-DXd for instance, that we've seen, which is another TROP2 antibody-drug conjugate that's given 1 week, once every 3 weeks, as

© 2023 ReachMD

opposed to 2 weeks and 1 week off with sacituzumab govitecan. And what would've been previously reported is that there were some patients, not all patients, but some patients, who received prior sacituzumab govitecan who had a response. So I think there's still some things that we need to understand about whether patients could have an antibody-drug conjugate that's targeting, that has the same target, similar payloads but different targets. There are lots of things that we'll need to figure out as additional agents come to treat our patients.

Dr. Bardia:
That's great. Lots more needs to be done in terms of ADC sequencing. And it's good to have more than one option. So, thank you so much for participating today. We covered "Optimizing Antibody-Drug Conjugates," the role of sacituzumab govitecan in the second-line therapy and upcoming therapies as well. Thank you. Thank you to the panel as well.

Announcer:
You have been listening to CME on ReachMD. This activity is jointly provided by Global Learning Collaborative (GLC) and TotalCME, Inc. and is part of our MinuteCME curriculum.
To receive your free CME credit, or to download this activity, go to ReachMD.com/CME. Thank you for listening.

© 2023 ReachMD