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# Expert Panel: Real-World Experience With ADCs in TNBC

**Announcer:**
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**Dr.Bardia:**
Welcome to this episode. In this episode, we'll review real-world experience with antibody-drug conjugates in triple-negative breast cancer. We have Dr. Kalinsky and Dr. Hurvitz. We'll have a nice panel discussion. So we'll start with Dr. Kalinsky. Dr. Kalinsky, you were involved with the clinical trial, the ASCENT trial, with trastuzumab deruxtecan even in the Phase I/II trial with trastuzumab deruxtecan and you've probably utilized the drug in the real-world setting as well. If you could share your experience both in the trial and in the real world setting with sacituzumab govitecan.

**Dr. Kalinksy:**
Yeah, so I think that one of the things just in terms of the efficacy that I always think is remarkable is that in the Phase I/II, we saw a really nice response rate of a third. And that response rate was recapitulated in a phase three trial. But beyond that, we saw an improvement in progression, free survival, and overall survival for about six months. And at ASCO, the data were presented with enough data, final analysis demonstrating that these consistent hazard ratios we're seeing with additional follow up. I think in the real world, my experience is similar to what was seen in the study and that the main side effects that I see patients facing is really neutropenia and growth factor utilization is higher than what we saw with chemotherapy. And that's certainly something that has held true. I think other sorts of side effects you know, nausea, diarrhea, preventing, if that side effect occurs, just making sure that patients have the appropriate anti-propulsive, etc. And I think the other thing that come I talk about with patients is just the alopecia. And I think the way that it was reported in the study underestimates the kind of alopecia that we see in my experience. All patients lose their hair. But I will say that in general what was reported in the study, I do think has been seen in real life as well.

**Dr. Bardia:**
Yeah, that's great. So there were no new surprises with utilization of the drug in real-world practice. Let's talk about another antibody-drug conjugate and we'll come back to real-world and let's trastuzumab deruxtecan. Dr. Hurvitz you were involved in the phase three trial with this agent and probably utilized this in real-world as well. So any differences in terms of clinical trial versus real-world practice with trastuzumab deruxitecan?

**Dr. Hurvitz:**
Yeah, in my experience the clinical trial really does sort of reflect how the drug is tolerated in the real world. In fact, I've only seen one patient who developed interstitial lung disease, and I've treated a lot of patients on various clinical trials DESTINY clinical trials, and then in real practice. And this was my first patient to have I.L.D was this past week. So I think that it, too is, is pretty well-tolerated overall. Patients will have hair thinning and I think that's not emphasized in the reports from the clinical trials as much. We're not as focused on that when we're looking at safety, but from a patient perspective, there's noticeable hair thinning. I've not yet seen full hair loss as we do with sacituzumab. I think the neutropenia can be an issue in some patients. You have to keep an eye on it. But nausea is the thing that I

think patients are most troubled by when they're being treated with this agent. And it's something that we really do need to pay attention to and use primary prophylaxis with the infusion. We have to arm patients with anti-emetics at home. There are some patients I've used drugs like olanzapine to help with this. Diet modification's also been helpful.

**Dr. Bardia:**
That's great. And in terms of pneumonitis I know that's been a big concern. Any changes from what it was first reported to now? Any value of early recognition? What's your practice?

**Dr. Hurvitz:**
Yeah, I think that's a great point. I.L.D in the DESTINY-Breast01 clinical trial was grade five in about 2.7% of patients. And that of course raised a lot of eyebrows and made us concerned. But when we looked at the DESTINY-Breast03 clinical trial the large Phase 3 clinical trial of T-DXd versus TDM one, there were no patients who died. And in fact, no grade four events and the total event rate was down to about 10.5%. This may reflect the very careful attention we were all paying to that potential risk, careful attention to the presence of ground glass opacities on re-imaging throughout the protocol and holding therapy even for asymptomatic I.L.D or grade one I.L.D until it resolves and permanently stopping with grade two I.L.D. I think the utilization of steroids or pulmonary consultation with our pulmonology colleagues, these are things that have helped us to deal with this. And then we saw the recent data relating to TDXD and the DESTINY-Breast04 clinical trial just presented at ASCO. And there, they did see a few patients. I think it was 0.8% or so grade five in this large clinical trial. Still, I think within the range of what is acceptable with a drug that has such profound efficacy, but does underscore the real importance that we have to pay attention to this and follow imaging closely in our patients not just send them and look again in four or five months. I think we have to more carefully follow the surveillance imaging.

**Dr. Bardia:**
That's a great point and the value of multidisciplinary management, getting pulmonologist ID involved as needed. Final question on pneumonitis TDXT, before we come back to sacituzumab govitecan and that's pulmonary function test. And the clinical trial pulmonary function test were required. But is that something you do in routine clinical practice?

**Dr. Hurvitz:**
No, actually we don't have evidence that PFTs at baseline are helping to predict for patients who would do better or worse with this. I think there are some studies going to look at whether following D LCO is going to be helpful. It's kind of like with trastuzumab, when it first came out in the use of echocardiogram, we've never shown that picking it up quickly, a cardiac event with echocardiogram. It is beneficial. And I think we're still evolving the best ways for us to detect and manage I.L.D at this point, I think the best evidence is to follow chest CT and patient symptoms very closely.

**Dr. Bardia:**
That's a great point. In clinical trials, we have stringent eligibility criteria number of tests that are needed but they might not be needed in real-world practice. So that's very valuable. And then finally on Sac--. There's an article on govitecan before we wrap this up and that's the use of biomarkers. Dr. Kalinsky do you consider UGT1A1 some data that could predict for AEs because SM 38 is metabolized via UGT1A1. So is that something you utilize in clinical practice?

**Dr. Kalinksy:**
Yeah, it was something that's been looked at, looked at in the study, and it did seem like maybe the rate of gastrointestinal issues were higher, but the take home point was to not necessarily prospectively evaluate for that with that particular assay. It's not something I utilize in clinical practice. I'll also say just in terms of safety, we also looked at those patients who were older, that were 65 years of age or older, just in terms of efficacy, as well as tolerability, with our potentially more fragile patients. And ultimately side effects were relatively the same. Efficacy was the same. So in my practice, I treat patients similarly regardless of age. And of course, that there are comorbidities and things like that. And of course, that's part of the consideration, but for a healthy, excellent performance status in a patient who's older, I will treat patients similarly.

**Dr. Bardia:**
That's very valuable to know regardless of age and you don't need to check for UGT1A1. Just start with the medication. And the final question, as we are on the biomarker topic of Trop-2, the antibody-drug conjugate targets Trop-2. So Dr. Hurvitz, any value of Trop-2 testing in clinical practice? You presented the results at San Antonio Breast Cancer Symposium a couple years ago. Is this something you utilize in clinical practice?

**Announcer:**
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