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Monitoring and Managing Treatment-Related Adverse Effects Associated With HER2-Directed Agents

**Announcer:**
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**Dr. Salani:**
This is CME on ReachMD, and I'm Dr. Ritu Salani.

**Dr. Pant:**
Hi. I'm Shubham Pant.

**Dr. Salani:**
Like any other cancer therapies, HER2-directed agents are associated with treatment-related adverse events. Shubham, what are some of the unique adverse events by tumor types?

**Dr. Pant:**
Ritu, thank you for asking me that question. I think it's a very relevant question nowadays. And let me just focus our discussion on antibody-drug conjugates because those are the recent approvals. They're kind of the newish kids on the block, at lease for folks like you and me, so we need to talk about these adverse events because folks who've not used a lot of these ADCs, like trastuzumab deruxtecan, definitely need to know the side effects and how to manage them.

Now the side effects, when I start patients on this, now these are targeted therapies so they're kind of – people call them as, oh, they're smart bombs, they're very targeted, they hit the cancer cell, don't hit so many things around, but antibody-drug conjugates are different. And when I talk to my patients I say this is probably like chemotherapy. It's not purely like trastuzumab single agent or trastuzumab/pertuzumab. This is like chemotherapy so you should expect the chemotherapy side effects. So expect the nausea, expect the anorexia, expect the vomiting, but most of them are grade 1 and 2 and they're tolerable, but it's also to set expectations for the patient, right. So if you have these side effects, do something about it. Just don't think this is going to be a walk in the park. It's real therapy. Now the other thing that they can face is just like regular chemotherapy, cytopenias. So heme toxicities, anemia, thrombocytopenia, and neutropenia. So that's important, and when we think about dosing and dose adjustments.

But one of the most important things I don't want anybody to forget is the serious adverse events, which is interstitial lung disease and pneumonitis because this can be fatal. So we really have to keep a close watch on our patients for developing this. So those kind of are the adverse events.

Ritu, how do you really manage these adverse events with HER2-targeted therapies.

**Dr. Salani:**
Yeah, thank you for that. I think that you summarized it so nicely. And I think one of the things is we're so excited about this new therapy

that's hitting marks that we haven't seen before in heavily pretreated patients, we sometimes overlook or minimize the treatment adverse related events. And I think one of the things to remember is checking the oxygen status, really asking patients about respiratory symptoms, shortness of breath, and really being quick to hold therapy or reduce dosing depending on what toxicity I see.

When I first used this drug, I actually partnered with one of my breast cancer colleagues because I was just like this is new and I don't want to overestimate kind of my experience. And I think it was really important. I learned a lot of kind of unique things that I added in addition to what we typically do with chemotherapy. But really monitoring these patients and I think setting expectations. We use a pretreatment antiemetic agent regimen that really helps kind of mitigate some of the nausea impact from these drugs. They are generally well tolerated, I will say, but you're right; it's a slippery slope. You can have shortness of breath that can then escalate to severe ILD, so it's important to really keep an eye on this.

**Dr. Pant:**
So, Ritu, ILD is such an important topic, important to our patients, important for clinicians, so how do you manage some of the side effects of ILD?

**Dr. Salani:**
So there's kind of 2 ways you can identify ILD. First, it can be asymptomatic with kind of findings on a CT scan. And if you do suspect it, which you should always have a threshold to suspect it, make sure you exclude other etiologies. It's not wrong to get a high-resolution CT scan, consult with a pulmonologist, and obtain cultures and looking for infection. Many other tests can be done as indicated.

If the patient's asymptomatic and it's a grade 1 ILD, you can actually hold the trastuzumab deruxtecan until the findings have resolved and then resume treatment once it has resolved. If it does take kind of 4 weeks to resolve, then reducing the dose will be critical.

If it's grade 2 or higher and it's symptomatic, it's really important that we discontinue trastuzumab deruxtecan permanently. These are patients that can escalate pretty quickly and have irreversible or even fatal consequences. Starting steroid treatment will also be important, and I often partner with my pulmonologist when we have pulmonary issues.

I just want to also highlight that patients with renal impairment may be at higher risk, so have different thresholds to monitor patients differently.

**Dr. Pant:**
Ritu, but this is not a new drug to our community oncologists, right?

**Dr. Salani:**
I think that's exactly right, and I think it just kind of shows the collaboration in our community where we each help other and learn from each other.

You know, I think this is a really great overview of the treatment-related effects, and I know it's been a brief but a really thorough discussion. So I hope we gave you something to think about and thank you for tuning in.

**Announcer:**
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