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Chemoradiotherapy Toxicities: How Do They Impact Starting Immunotherapy?

Announcer:
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Dr. Reuss:
Hello, this is CME on ReachMD, and I'm Dr. Joshua Reuss, and today we're going to be discussing chemoradiotherapy toxicities and how they impact the start of the all-important adjuvant immunotherapy.

So in my discussions with patients, I tell them that in the world of lung cancer, chemoradiation is one of the hardest treatments to go through. Whether it's sequential or concurrent, it's long, it's exhausting, and then the toxicity profile can take some time to recover from. What are these toxicities? So in addition to just the fatigue of good day-to-day going through therapy, oftentimes we encounter esophagitis and odynophagia, the severity of which, in my view, really depends on the radiation field and what's being targeted. If this is a more peripheral area of disease, oftentimes the radiation field does not significantly overlap with the esophagus, and we see a lot less esophagitis. However, in patients that have a high burden of mediastinal lymph node involvement, oftentimes there is a lot of the esophagus that's involved. And so in order to predict that, I'm oftentimes talking with our radiation oncologists, trying to get a sense for the radiation field. And then obviously, seeing the patients regularly to see are they having any problems with swallowing? Are they having any barriers to appropriate nutrition because, obviously, that impacts a lot in terms of one's ability to get along day-to-day, their strength, their functionality, that can impact the start of adjuvant immunotherapy.

We do worry about cardiotoxicity depending on the radiation field. I tend to see that more as a later-onset side effect that typically will not impact the start of immunotherapy. And obviously, the extent of cardiac overlapping with radiation will oftentimes impact the radiation oncologist to perhaps push for proton therapy over more standard IMRT [intensity-modulated radiation therapy] techniques.

But I would say that one of the biggest toxicities that we encounter or that we look out for in terms of starting immunotherapy and then navigating immunotherapy is pneumonitis. We do know that any-grade pneumonitis appears to be higher in this setting of post and peri-chemo RT than in the metastatic setting with systemic immunotherapy, where any-grade pneumonitis in the PACIFIC study was seen at 34%, though high-grade, you know, relatively low, maybe 3.5%. But this has been replicated in real-world studies where we've seen any-grade pneumonitis and ILD ranging from around 18% up to 20%, 25%.

So how do we mitigate this? I think one of the important first steps is determining what do we think is the etiology of pneumonitis. If limited primarily to the radiation field, this is oftentimes more related to radiation. Other things go into that in terms of timings from radiation, but oftentimes those are scenarios where, depending on the symptoms and degree of involvement, if symptomatic, we may take a pause in immunotherapy, if already begun, start steroids, and then reassess. Sometimes, though, if it's very limited in terms of the inflammatory changes and the patient has no symptoms, I'll continue immunotherapy. And in reality, because we get scans so soon after completing chemoradiation, within a couple weeks, oftentimes we don't see those inflammatory changes initially, but they appear in subsequent scans on immunotherapy, but based off of the location and the extent, oftentimes these are limited, related to radiation, and don't warrant a hold of immunotherapy.

We see scenarios where more widespread pneumonitis develops, and in those settings, oftentimes it is related to immunotherapy. In these scenarios, I want to make sure to rule out other common things, infection, disease progression, but if it ultimately is felt to be related to immunotherapy, putting a hold on the immunotherapy and starting appropriate steroids is definitely the best next course of action. And then, depending on the severity, was oxygen requirement needed? Was a patient hospitalized? Oftentimes, those are factors that go into whether or not immunotherapy can be safely resumed. Typically, if someone does have severe pneumonitis where they now need oxygen when they previously did not or they need to be hospitalized, I will typically halt immunotherapy going forward in those scenarios.

Who is at risk for this immunotherapy toxicity is a really important topic of research, and I think the data is mixed. I don't tend to believe that the timing of radiation to immunotherapy start impacts this. Multiple retrospective and real-world analyses suggest that timing to IO start does not significantly impact the risk for pneumonitis development. But I think we definitely need more data to see who is at risk for developing pneumonitis and how can we appropriately monitor for that.

So with that, I know that was a highly complex discussion and very important in managing our patients. But I hope that was something that was useful and I want to thank you for your attention.

Announcer:
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