Transcript Details
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DESTINY-Breast05: Additional Data From the Interim Analysis

Announcer:
Welcome to DataPulse from San Antonio Breast Cancer Symposium 2025 on ReachMD. This activity, titled “DESTINY-Breast05: Additional Data From the Interim Analysis” is provided by Global Learning Collaborative.

Dr. Geyer:
Hello from San Antonio Breast Cancer Symposium 2025 here in San Antonio, Texas. I'm Dr. Charles Geyer, and today I'll be reviewing additional data from the DESTINY-Breast05 interim analysis that were updated here at the conference.

We actually reported the DESTINY-Breast05 primary results a few months back at ESMO 2025 after we crossed the early reporting interim boundary. DESTINY-Breast05 was developed as a straightforward study that attempted to address unmet needs we identified from the KATHERINE trial. KATHERINE was great. It improved outcomes, reducing risk of recurrence by 50% virtually in all groups, but some of the groups had such a high risk for developing recurrence that even with the 50% risk reduction, they still had an elevated risk of recurrence. So we had this high-risk group with this unmet need. We also saw that T-DM1 didn't impact on the problem of brain mets.

So DESTINY-Breast05 basically took those patient groups, those who presented originally with inoperable cancer or those who still had positive lymph nodes after surgery, and randomized them to receive standard 14 cycles of T-DM1 or 14 cycles of T-DXd.

What we showed at ESMO was that T-DXd resulted in a 53% reduction in risk for IDFS events with basically 30 months of median follow-up. So we saw a very early separation of the curves that widened over time. So clearly a positive trial.

On the study of course, one of the concerns we have that we all recognize with T-DXd is the potential for ILD. We had safety studies built into the trial of getting serial CT scans—non-contrast, low-dose CT scans—screening for ILD that were there on both arms. So we were very careful about identifying ILD and hopefully identifying it early enough to interrupt therapy, treat with steroids as needed. So a key part of it was our safety data.

How often did we see ILD? Overall, we saw 9.6% of patients getting 14 cycles of T-DXd develop the ILD. Fortunately, 8.5% of those were grade 1 or grade 2, and the majority were resolved or resolving at the point of the data cutoff.

What we were able to present here at San Antonio was information looking at additional subsets that we didn't have the information on with the initial analysis. Anytime you see a positive result in a composite endpoint like IDFS, you want to look at subsets to see is it consistent across the groups? And we had shown that for our stratification variables, whether patients had received one or two HER2-targeted therapies, where they had presented with locally advanced or were node-positive disease, nodal status, hormone receptor status; all those, there was no difference.

The thing we hadn't looked at and were curious about, of course, was what about IHC 2+. We've seen it with T-DM1. Patients with IHC 2+ cancer don't seem to derive as much benefit from T-DM1 as we would like to see. So Dr. Loibl presented data showing that, indeed, with T-DXd relative to T-DM1, there was a marked improvement in outcome. The improvement there for that subset, we had a hazard ratio of 0.35. So we now see an unmet need being met by the improved outcome of patients who have HER2 IHC 2+ status and otherwise meet the criteria.

We also saw—to me, not surprisingly—that whether they got an anthracycline-containing regimen or not, they benefited from the therapy. Dr. Loibl also provided an update on the more breakout of the ILD information that I think was useful.

And then the new information was onset of ILD. Since we do 14 cycles, since we had this 9.6%, there was the obvious question of, well, when do you start seeing it? Is it a cumulative risk the whole time you're treating? And what we saw was that the range was 36 days up to 350 days, and the median was about 120 days. So it is apparent that the longer you're on it, the more toxicity risk you have for the ILD.

And I think particularly since we've seen with the shorter use in DB11 in the neoadjuvant setting, 4 cycles, half as much, I think this will be a continuing developing story as to how much T-DXd do you need in the early setting, and we'll work to try to minimize that risk.

So I think what we've learned is that we have shown unequivocally that T-DXd is a very effective therapy for high-risk patients to maximize their chance for being cured of cancer. But you do have to respect the potential for the ILD.

So from San Antonio Breast Cancer Symposium 2025, I'm Dr. Charles Geyer. Thank you for listening.

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