Transcript Details
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GEP Testing for Cutaneous Squamous Cell Carcinoma

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Cutaneous squamous cell carcinoma is the second most common skin cancer in the world. And one of the challenges is identifying which tumors we have to be more worried about. And so historically we've used our staging systems and then the NCCN guidelines, which help us to risk stratify tumors. But even within staging systems, we still fail to identify about 30% of the outcomes which occur in the low-stage tumors. And so the 40-GEP test tries to enhance our ability to identify which tumors we have to be most worried about. And so when you send off this test, you get back a result that's either a Class 1, which is lower at risk; a Class 2A, which is in the middle; or Class 2B, which is the riskier result.

So the 40-GEP test from Castle Biosciences is actually the only test of its kind in cutaneous squamous cell carcinoma at the present moment. And when they first developed the test, they did it on cutaneous squamous cell carcinomas that had what they defined as one risk factor. But I will say that a lot of the tumors they used to develop the test were low risk in my opinion. They would be staged as Brigham and Women's T1, or they would be an AJCC 8 T1, so the lowest stage invasive squamous cell carcinoma.

We've developed a dataset along with Cleveland Clinic that has tumors that have at least one risk factor that we defined that is a little bit riskier. So these would then be Brigham and Women's T2a tumors, so the next level up from what they initially used. And then we've done several studies to not only validate the test just in different populations such as in general or head and neck squamous cell carcinomas, but we've also done some studies looking at how to utilize it in clinical practice.

So one example was that we looked at Brigham T2b tumors. So these are two risk factor tumors, the classic risk factors that we think about for our staging systems. And we looked at what percentage got imaged in clinical practice. And then we looked at the risks associated with the classes, and we saw that the Class 1 for Brigham T2b in our cohort actually had about a 5% risk of metastasis, whereas the Class 2A was closer to 20% and the 2B was even higher. And so we were able to say, well, maybe for the Class 1s you don't have to do imaging and the other, 2A, 2B, you would do imaging. And actually we saw that fewer patients would've required imaging overall. And so that's one use case for the GEP.

We've also looked at utilization for adjuvant radiation, and there have been two studies, one of which I was not involved in, that showed that for the 2B results, there was a 50% reduction retrospectively when they implemented this retrospectively in outcomes with radiation. But we didn't see that with the Class 1 or the 2A. Now in contrast, the study that I participated in of looking at radiation, a very similar methodology, but again, the cohort was higher risk, actually saw a 30% reduction with the 2As, and 50% reduction with the 2Bs for radiation.

So there are several caveats, I think, to these two studies. The first is that the different results really highlights the importance of looking at a risky enough population that would warrant radiation to begin with, because we shouldn't just be using the test to guide radiation even if there's a T1 that gets a 2A, 2B, it doesn't necessarily mean that that's the appropriate treatment. And so we really want to identify patients where you think that this test can help guide radiation one way or another.

The second caveat is that the GEP test only looks at metastasis. It does not look at local recurrence. And for the most part, adjuvant radiation is delivered really to reduce the risk of local recurrence because you're localizing it. There is some data to say maybe it also reduces local regional recurrence, but I think for the most part, we really think it's for local recurrence. And so that's another caveat to these two studies.

I personally think that we really need to identify this intermediate risk group that would most benefit from additional GEP testing. We

know that there are very low risk tumors that maybe a handful will develop outcomes, but it's quite rare, well under 1%, maybe even well under 0.5%. And then there are tumors that are super risky that we know their risk is already based on their clinical risk factors very high. And so really we want to focus on this intermediate risk group where we're not sure if they're going to be bad actors or not. And then that's the type of tumor where it could possibly benefit from gene expression profiling. And I think this is a great future area of research, is really to look at what is that intermediate risk group who would most benefit, and that data I think could be really helpful in clinical practice.