GERARD SILVESTRI: Our study was on a new biomarker, an integrated biomarker that is used to help distinguish cancer from not cancer in patients who have pulmonary nodules. It was published in our journal CHEST this past month. The paper basically looks at the use of a blood biomarker to help distinguish cancer from benign disease in lung nodules. It was a 30 site study nationally in over 680 patients. What the study found was that, in a group of patients where physicians thought their predicted probability of cancer was less than 50% and they had a negative blood test, those persons could be reliably told that they did not have cancer.

Why is that important? It's important because many patients with these small lung nodules have to go through biopsies and lots of other testing up to and including surgery when they might have a non-cancerous spot in their lung. So, with the addition of the usual clinical predictors of cancer, a blood test that shows no cancer in patients with less than 50% chance of having cancer in their lung nodule is really a big important advance in how we approach these patients.

Patients with a lung nodule when they come to my office, it's really my job to be able to offer them options. One option would just be to follow them with surveillance. That means getting CT scans of their chest to see if the nodule is growing. The next option would be to do a biopsy either through a bronchoscopy internally or numbing up the skin on their chest and doing needle biopsy or being directed directly to surgery in those nodules that look high enough risk that they're cancer that we just feel they have to come out.

The dilemma is knowing when to do which test. Most of that's based on clinical intuition-- do we think that they're the right age group; do they have a heavy smoking history, which would make cancer more common; what are the characteristics of the nodule on CT scan? Once we accumulate that information we would go ahead and group them or make recommendations based on each of those buckets I talked about. We also, of course, invite patients to be part of the decision.

Some patients, even if you tell them there's very little likelihood that this is cancer, they still seem to want it out because they may have had a relative with cancer or just can't sleep at night not knowing what this is. Other patients are a little bit more tolerant and want to watch it for a little while, even if I thought it might be cancer.

So that's the dilemma that we have. Adding an additional piece of information like what this integrated biomarker does for us I think can help. It's another piece of information that, particularly when it's useful, that can tell us, hey, this might not be cancer. Really you shouldn't do any further testing but watch the nodule.

The classifier is really what's called an integrated classifier. It uses two proteins that help distinguish cancer from non-cancer, but it also incorporates some of the things we know about predicting cancer, like age of the patient, size of the nodule, whether the nodule has certain characteristics on radiograph. So it's an integration of clinical parameters plus these proteins that can be found in the blood.

What we found in the study is that it's a good test at ruling out cancer, but it really doesn't help you to rule in cancer. So in those patients where we think there's a good probability that they have cancer and if they were to have a "positive test", we don't think that should affect their care. And if they have a negative test, we don't think it should affect their care. If you think that there is a good chance this person has cancer, they should go on and have some type of invasive procedure, whether it be a biopsy or a lung resection because, what you wouldn't want to do-- it's really important not to miss cancers when they're there. So this is really a good rule-out test in those with a moderate to low probability of cancer, but not a good rule-in test.

The next step would be what's called a clinical utility study. What that means is, in this first trial the doctors were completely unaware of what the blood test showed. So they never were able to act on the results of the blood tests. It was a validation trial. And after the trial was ended, did we know which patients had cancer and which didn't and which had a positive blood test and which didn't.

The next piece of research is what's called a clinical utility trial. That is, when we see a new patient with a nodule in that category of moderate to low probability cancer and we draw the blood test, then we would act on the blood test. We'll get the results back, and then we'd be able to act on the blood test to see if it really changes how physicians and patients behave in terms of lessening the invasive diagnostic testing for those with benign disease and so forth.

So what we really want to do is-- the next step would be to do a clinical utility trial to tell us, hey, look like this is useful in reducing unnecessary testing for benign disease. Which this study showed that, hypothetically, if we had followed the results of this test, about a third of the

time we would have avoided invasive and unnecessary testing in our patients which would be really good for patient care.

The message I'd give to clinicians about this study is twofold. One is I think we now have additional tools we can use to help manage nodules. But, the first message is that there are good guidelines for how we manage nodules, and physicians don't always follow them. So it'd be really nice if they both followed the guidelines, but this may help build their confidence in taking into account whether the patient has cancer or not.

So, just again, if the patient has a moderate probability of cancer and the physician gets back a negative test, they should have confidence that it is very unlikely that that patient has cancer and they could afford to get a CAT scan in three to six months to see if the nodule is growing. There's a lot of biomarker work going on out there. So this may not be the only biomarker we see. There are other companies and folks at the NIH and National Cancer Institute working on biomarkers to help distinguish cancer from not cancer. So this is the first one to reach this level of testing.

But, I think there'll be others in the future. And, of course, a rule-in test would also be nice, right? So if we had a biomarker that could tell us, hey, look you need to get moving here. This patient might have cancer. And so, that would be another nice biomarker for the future.