TuSalud

Biomarkers, Tumor Markers and Tumor Boards: What Cancer Patients Need to Know

Cancer care is changing — as are the clinical tools, tests and the terms used to diagnose and predict its path and treatment.

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When Ginny Mason was diagnosed with inflammatory breast cancer in 1994, she never once heard the word “biomarker.”

“Back then, all you got was ER and PR [the estrogen receptor and progesterone receptor] — HER2 hadn’t been discovered yet,” said the 72-year-old nurse and executive director and co-founder of the Inflammatory BC Research Foundation. “There wasn’t even an internet when I was diagnosed.”

Mason’s doctors told her she was negative for ER and PR, so she knew she wouldn’t be put on anti-hormone, or endocrine therapy. Other than that, “biomarkers and biology were really not talked about,” she said. “And there were only three drugs available.”

Thirty some years later, Mason is still here to advocate for other cancer patients — and to witness and help translate the massive changes that have taken place since her own diagnosis.

“It’s a very different world now in cancer,” said Mason. “Now you need to understand the subtype of your breast cancer. You need to know what your biomarkers are so you can get the appropriate drugs. In many respects, it’s more confusing because there’s so much information out there. It’s hard to sift through it and know what’s important. We talk a lot of about shared decision-making — but you don’t know what you don’t know.”

Curious about what you don’t know about cancer therapy these days? Let’s look at some of the ways cancer care — and even the terms used to describe it — are transforming at Fred Hutch Cancer Center and beyond.

What are tumor markers?

For years after treatment, Mason’s doctors tested her blood to assess her tumor markers, making

sure her treatment worked.

But what are tumor markers? And how do they differ from, say, biomarkers?

“The terms are not interchangeable,” said Fred Hutch breast cancer oncologist and researcher Natasha Hunter, MD. “Tumor markers are molecules, often proteins, produced by the body or by cancer cells that are measured, often with a blood test.”

Tumor markers are a subset of biomarkers, Hunter said, but they’re “not very specific and they’re often not very sensitive.”

Some of her metastatic breast cancer, or MBC, patients’ tumors will grow or shrink but their tumor markers “remain completely flat and nonresponsive,” she said. “In other patients, when their markers start marching up, that’s a sign of progression.”

Case in point: CA-125 (the CA stands for cancer antigen) is a tumor marker for ovarian cancer, but it can also be elevated due to inflammation from endometriosis, liver disease, inflammatory bowel disease, pregnancy or recent surgery. In an effort to uncover more reliable markers for this disease, researchers from around the world, including Fred Hutch’s Holly Harris, PhD, ScD, created PREDICT, the Prospective Early Detection Consortium for Ovarian Cancer.

The uncertainty around certain tumor markers is most likely why the National Comprehensive Cancer Network’s (NCCN) guidelines, which standardize much of cancer care in the U.S., don’t recommend using them in early-stage breast cancer.

But many clinicians measure them anyway, often to provide peace of mind to their patients.

“Our group at Fred Hutch does not use them for early-stagers,” Hunter said. But they use them regularly in MBC patients, after first verifying the markers are reliable.

“If the scans are stable but the tumor markers bounce around, I’ll know they’re not useful,” she said. “But if they only rise when the cancer starts growing, that gives me a sense they’re useful in that person.”

Fred Hutch gastrointestinal oncologist Gabriela Chiorean, MD, said pancreatic tumor markers are also problematic.

“It’s not like a specific marker just for cancer,” she said. “That protein exists in healthy people, too. A patient may come to you with COVID, or a bronchial infection, and their markers are through the roof, so they think their cancer’s come back, but it’s just inflammation in the body.”

Tumor markers can also rise due to diarrhea or uterine fibroids or low thyroid function or infection or a biliary obstruction due to a gallstone, she said.

Common cancer tumor markers include PSA (the prostate-specific antigen); CA 15-3 and CA 27-29

for breast cancer; CA 19-9 for pancreatic cancer; BTA (bladder tumor antigen) for kidney, bladder or ureter cancer; BCR-ABL for leukemia and lymphomas and CEA, or carcinoembryonic antigen, for colorectal cancer.

What are biomarkers?

More and more, cancer care is evolving with treatments designed to target the genetic or molecular makeup of a cancer. That's where biomarkers come in.

This term covers a much broader category and can include genes, gene mutations, proteins or other substances that can be measured in blood, tumor tissue or other body fluids.

Why collect and analyze these signals? They provide crucial information about a patient's health.

Biomarkers aren't limited to cancer but often provide key insights regarding a person's cancer (or their risk of it); they can also inform treatment decisions and predict prognosis and/or recurrence. Some can even tell if a patient will respond to a treatment or not, saving them from unnecessary side effects and ineffectual therapies.

What's tricky for many, especially those new to the world of cancer, are the various terms used to describe biomarker testing.

Doctors might refer to it as tumor testing or tumor genetic testing or tumor subtyping or genomic profiling or sequencing. They might also mention molecular profiling or molecular testing, somatic testing or next generation sequencing, or NGS.

Hunter said biomarkers are the answers you get to "a lab test, an imaging test, any test to check on the status of the tumor. It's a biological metric that answers a question. It could be a blood draw or even a scan."

Biomarkers can even be a combination of test results, she said.

"I would call Oncotype Dx a biomarker test," she said. "It's a combination assay that looks at gene expression and DNA sequencing to answer the question, 'Should I give this patient chemotherapy?'" Other tests that look for breast cancer biomarkers include Mammaprint and Prosigna; another test, Cologuard, looks for biomarkers of colorectal cancer.

Chiorean said biomarkers often reflect molecular signatures or profiles.

"We do a biopsy or identify tumor DNA from a blood sample and then we sequence it to look for mutations," she said. "Chemotherapy will kill indiscriminately, but checking the genetic signatures and profiling with next-generation sequencing (NGS) tells you what type of mutations are present in the tumor. This is essential to determine what treatment options are unique to the tumor."

Useful biomarkers in breast cancer include ER/PR status, HER2 protein expression, Ki-67 (a cell proliferation biomarker) and various genetic mutations including ALK, ATM, CHEK2, PTEN, BRCA1/2 and others. EGFR, short for epidermal growth factor receptor, is a common biomarker in non-small-cell lung cancer. BRCA1 and BRCA2 are biomarkers for prostate, pancreatic, ovarian and breast cancers. And there are many other assays, molecular tests and scans that produce additional useful biomarkers.

Chiorean said molecular tests allow clinicians to "offer patients many more treatments." But not all cancers have consistent, reliable biomarkers to inform treatment or reveal the aggressiveness of the disease.

Sid Sadler, a 33-year-old social media manager from Nashville, Tennessee, said there aren't reliable biomarkers for his clear-cell renal carcinoma, which he refers to as the "Honda Civic of kidney cancers" because it's so common. (As with many solid tumors, there are several subtypes of kidney cancer.)

But studies are underway to ascertain whether KIM1, short for kidney injury molecule one, might serve.

"For the longest time, they would see this molecule in kidney injuries, in people hurt during sports," Sadler said. "But now they're thinking it could be prognostic — predict recurrence — and could be useful before or after surgery to see if KIM1 was in the tumor."

Sadler said having such a biomarker would be extremely useful, because "if a tumor has more KIM1 or it's expressed more, clinicians might want to look at adjuvant therapy," meaning additional treatment given after the main treatment.

What's a tumor board?

Mason, the breast cancer patient, didn't have access to biomarker tests or genomic profiling to shed light on her disease back in 1994, but her doctor was able to tap a long-held medical institution known as a tumor board for their insights into her cancer.

Tumor boards are basically a "recognition of the power of many minds coming together," Hunter said. And they exist in most tumor types.

Mason said she was able to access the NCI's tumor board, which recommended she do neoadjuvant chemotherapy based on a "newly published study that found aggressive cancers in general might be better controlled with chemo before surgery."

Hunter said within Fred Hutch's breast cancer program, there are three types of tumor boards. One meets twice a week and is designed exclusively for newly diagnosed early-stage breast cancer patients.

“This is something Fred Hutch does that most other institutions don’t do,” Hunter said. “We all come together and figure out how to cure that cancer — medical oncologists, surgical oncologists, radiation oncologists, radiologists and pathologists, along with nurse navigators and other supportive staff.”

Patients generally aren’t present at tumor boards, due to the technical nature of the discussions, though patients will often meet with multiple specialists during an appointment, who separately discuss treatment options before presenting them back to the patient.

“We’re using jargon, and some things might be hard for patients to hear,” Hunter said of tumor board discussions.

But patients benefit from “having all these people at one time discussing their case.” And studies show they improve outcomes, too.

“We look at the patient’s radiology, mammography, MRI and other relevant imaging,” she said. “The pathologist brings up slides of the tissue and we look at that. Then we have a conversation about the best strategy for treating the patient. It’s sort of a one-stop shopping experience for patients.”

The second type of tumor board, the standard breast cancer tumor board, she said, is for more complicated, often metastatic, cases.

“Sometimes a patient will have complications or other medical issues that complicate care or there’s a weird finding,” Hunter said. “That’s when you come to this tumor board with all the key players.”

What’s a molecular tumor board?

The third — and newest type — is the molecular tumor board.

“As we move forward, we’re not only talking about DNA, but also RNA and about proteins that are being expressed by the patients’ RNA,” Hunter said. “We look at tumor tissue under the microscope — and we look at DNA at the molecular level. And both can guide treatment.”

Molecular tumor boards include the “same group of smart people,” Hunter said, along with molecular pathologists who will talk through all the various mutations and pathways.

“We’re at the start of a new era in understanding cancer on a molecular level,” she said. “Tumors will have mutations that represent pathways it uses to grow and divide and avoid immune detection.”

Cancer cells commonly hijack certain kinds of genetic codes — blueprints for growth and development — and use them for their own benefit.

“The cancer may start growing out of control and remain active despite getting signals to stop,” she said. “It can send off cells to set up camp in other parts of the body and cause metastasis. It can de-differentiate so the cells will behave in ways that breast tissue should not behave.”

And once you have cancer, the cancer cells can encourage additional mutations to happen. Eventually, cells may lose the ability to repair themselves. Tumors may develop a host of mutations.

Most large cancer centers can now sequence a tumor’s genome in hours, unlocking information on the tumor’s mutations and pathways — and how to target and block them.

“If a mutation is taking a particular access ramp off the highway to get into the neighborhood and cause problems, we can block that exit ramp,” Hunter said. “But if we don’t know that road is there, then we can’t use it to cut off the tumors’ access.”

Both Hunter and Chiorean said molecular tumor boards almost always look at metastatic cancer cases.

“We have molecular tumor boards for every cancer — colorectal, pancreatic, neuroendocrine, etc. — and usually meet once a month,” Chiorean said. “We also do molecular profiling for every metastatic cancer patient and discuss the tumor’s profile. What does it mean? What treatment options does the patient have?”

But it’s not as simple as matching a particular mutation to an approved targeted therapy.

“It’s definitely more complicated,” she said. “Some mutations work in tandem with others to create a certain environment. Sometimes, you have to use a combination of therapies to attack that mutation.”

And assumptions are risky.

“Just because it works in ovarian or breast, you can’t assume it will work in gastrointestinal cancers,” she said. “For every genetic mutation, we need to study every cancer separately in cell lines, preclinical tumor models and then in clinical trials to see what works best.”

In addition, efforts are now underway to make molecular tumor boards — and the precision treatments they pinpoint — more widespread and accessible to community oncologists and cancer centers.

All in all, Fred Hutch experts agree there is much more to do in the realm of precision oncology.

“We are in search of better biomarkers and better tumor markers that have more utility for more people,” Hunter said. “In some ways, what we know is amazing and extremely granular. But in other ways, we know way less than we should. If I could cure my way out of a job, I would love it.”

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