The Democratization of Precision Medicine: A Clinician's Perspective on the Future of Oncology Care

Q&A With Neil Vasan, MD, PhD

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***AJMC®*: What are your impressions regarding the rapid evolution of the precision medicine landscape, and how does it affect your approach to care?**

VASAN: When it comes to precision medicine, or personalized medicine, some semantics are at play. Certain cells are sometimes more susceptible to chemotherapy, and therefore one could argue that chemotherapy is precision medicine. Many of our early therapies, like tamoxifen and aromatase inhibitors, are targeted therapies. They target the estrogen receptor, and we give them to patients whose cancers have elevated amounts of those estrogen receptors. In some sense, the modern targeted therapies are just an interpretation of what we have already been doing in the field. I am a breast oncologist, and we have been the beneficiary of many targeted therapies, such as antiestrogen therapy, and newer antibodies, such as trastuzumab and pertuzumab, and most recently cyclin-dependent kinase 4 and 6 inhibitors and phosphoinositide 3-kinase [PI3K] inhibitors. Many of these drugs improve overall survival in our patients. Because we have biomarkers for these targets, it's wonderful to know patients who would receive the highest benefit from these drugs and those who may not. Certainly, in colon cancer we have certain biomarkers that predict for lack of responses to drugs. Thus, being able to fine-tune which patients may or may not benefit from these drugs is critical to moving this field forward.

***AJMC®*: How important do you think this kind of terminology is when it comes to defining the lines of precision medicine?**

VASAN: It's really important to let the general public know that these are really exciting therapies and diagnostics and that they represent truly cutting-edge science and have become a standard of care. This shows the public why what we do is important, why what we do as clinicians is important, why what we do as scientific investigators is important, why it merits funding, why it's in the national interest, and why the government should be investing in scientific research.

The flip side is that we should not overhype or oversell what these personalized approaches can and cannot do. That's important because many of the therapies in this realm of personalized medicine and targeted therapies can have really small responses. That doesn't mean that it's not important; many times, the small responses are in diseases that are otherwise totally intractable or diseases in which so few therapies are available that any advance is notable. Nevertheless, it's important not to oversell and to be really honest about what these therapies can do.

Often there is big chasm between the advances made in science and how they really enter the clinic. In oncology, we are very fortunate because so much of the basic science does translate into therapy. Thus, what personalized medicine really means is that the therapies being given are commensurate with the level of basic science that's happening at that time.

***AJMC®*: Can you talk about the approach to precision medicine at Memorial Sloan Kettering Cancer Center (MSKCC) and your role there?**

VASAN: We are fortunate at a place like MSKCC, where we have access to all the FDA standard-of-care treatments. We also have access to a tremendous number of clinical trials. Many of those clinical trials that are testing the most promising drugs coming out of the preclinical studies are phase 1 studies. Many of those drugs are targeting specific mutant proteins, and we are also able to do testing that has never been possible before. Sometimes these altered proteins are mutated proteins in a particular cancer; therefore, finding patients who have a particular change may actually tell us something different about the disease.

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***AJMC®*: Can you talk about what you're seeing in the general oncology world beyond MSKCC as this field is changing?**

VASAN: One thing we're seeing is a democratization of testing techniques. For instance, many years ago, testing was made available at large academic centers only. Now, through collaborations with the private sector, companies are testing both tumors and blood for things like circulating tumor DNA. This has really opened up the diagnostics for patients who may not have access to a large academic center, and it has also opened up the possibilities for enrolling in clinical trials. From the treatment point of view, certainly many of the cooperative groups are starting to open trials that reach the community as well. We are also seeing that many academic centers are opening satellite facilities that are affiliated but are closer to the community, allowing patients to get treatment closer to home and, in some cases, access to clinical trials much closer to home.

***AJMC®*: How would you describe your relationship with those on the pathology and testing sides of the spectrum at MSKCC?**

VASAN: It's a very collaborative, respectful relationship. We all bring different pieces of the puzzle to the table, and we all have preening and expertise. We really rely on our colleagues for some of those really fine-tuned diagnoses. In breast cancer, the pathologic diagnosis is almost always given by an outside facility. We rely heavily on our pathologists. They really are the experts in interpreting everything that we do. One thing that's really great about oncology is that we often have time to make the right decisions. We don't have to make acute, rash decisions, and by having time, we can enlist all our colleagues.

***AJMC®*: Do you see any particular challenges in either the testing or therapeutic side regarding selection of the proper intervention?**

VASAN: I think there are 2 main challenges. One is a time limit. Some tests can take time. Some tests take 1 or 2 weeks, whereas others take 4 weeks. If you really need to start treatment as soon as possible, that may influence the type of testing that you're sending out, noting that for the vast majority of cancers, this testing is really cutting-edge; it's not necessarily the standard of care, but it's something that has novel therapeutic options.

The second challenge is implementation—specifically, ensuring that pathology for the patient who has metastatic cancer or has been on X number of lines of therapy is reviewed by the institution, that radiology has been reviewed, and that all appropriate testing has been done. That testing can be standard DNA sequencing, or it can be more sophisticated. In an ideal scenario, when we are starting to get all that data together, all of that would already have been sent out before we see the patient, so we would get all that data on day 1 when we see them. Right now, we get that information piecemeal. Maybe some of this should be centralized by either a company or an institution because that would really help the decision making.

***AJMC®*: What are the managed care implications of the growing diagnostic market?**

VASAN: I order tests only if I'm going to act on that knowledge and if the knowledge is meaningful. We are fortunate in breast cancer because we have certain therapies we can rationalize to the patients and with insurance companies to do certain types of testing. For example, *PI3K* mutations are very frequent in breast cancer, and we now have a PI3K inhibitor [alpelisib] that's FDA approved. One test that I order routinely on patients with metastatic estrogen receptor–positive breast cancer is a circulating tumor DNA test. There are also tests available to determine if a patient has an *ESR1* mutation. If patients have it, they probably would have resistance to aromatase inhibitors. The reason that's an important test, as well, is that many of our patients have bone metastases only, and with bone biopsy, it can sometimes be very challenging to get this type of data from the tissue itself. That's why these

liquid biopsies are extremely helpful. I have never had a single case where it's been denied by insurance. My understanding is that most insurance companies approve tests for patients in this scenario. Therefore, the onus is really on physicians to identify who these patients are. We have to be judicious about ordering these tests, knowing that if we get a piece of data, we should really think about acting on it.

***AJMC*®: What kind of opportunities do you foresee based on the evolution of precision medicine testing and therapeutics?**

VASAN: We need more harmonization when it comes to these types of testing. Perhaps we also need clearer guidelines from societies like the National Comprehensive Cancer Network regarding when to use this type of testing, when it's appropriate, when it's not appropriate, etc. Some of these organizations can have a 1-size-fits-all approach to recommendations but need to be very specific in their language. White papers from the societies reviewing when to get these types of testing would be helpful. One thing that is challenging is [the potential for] significant variation in quality and expediency regarding testing results; many institutions have preferred vendors, but more harmonization regarding certain vendors or certain techniques, or even studies that compare different companies with [one] another, would be very helpful in getting the highest-quality data. ◆