Multidisciplinary Panels: Putting Sequencing Data to Work

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The use of genomic testing in clinical practice is increasing, but interpretation of results can be a challenge for many oncologists. Multidisciplinary tumor boards can help clinicians and patients sort through the large volume of information that is generated by genomic testing. With the interpretive help of a tumor board, oncologists can weigh available options and translate the genetic information into informed decisions on patient care, according to speakers at an Extended Education Session, "Expediting the Learning Curve for Applied Cancer Genomics," on Friday, May 29.

Dr. Eliezer Mendel Van Allen

Only a few years ago, discussion of genetics would have been rare at an ASCO Annual Meeting, session Chair Howard L. McLeod, PharmD, of Moffitt Cancer Center, said, but "now its double helix is woven throughout everything we do."

An understanding of genomics has become essential in many aspects of oncology practice. In striving to achieve personalized cancer care, information from the tumor and germ-line genomes can be used to select treatments and explore clinical trial options, he said. When multiple treatments are available for a given disease, a tumor panel can help with selection of the best therapy among seeming equals—the one most likely to be efficacious for the individual patient.

The session featured discussions of how to apply information from deep sequencing, what to do with incidental germ-line findings, and informatics strategies to turn sequencing data into patient care. The centerpiece of the session was a pair of presentations on how multidisciplinary tumor boards can be useful to augment the value of cancer sequencing.

Value of Tumor Boards

"Genomic testing is here; we're using it. It's just a matter of what to do with the information. The information is not going to get simpler; it's going to get much more complex," Robert R. McWilliams, MD,

of Mayo Clinic, said. One way to derive more value from sequencing data is to take advantage of the broad range of expertise brought together on a multidisciplinary board.

Dr. McWilliams described the results of an informal survey he distributed among colleagues at Mayo Clinic and its affiliated health system to see whether the respondents would view a tumor board as a valuable resource. The first question was, “Have you used genomic testing in your practice beyond standard-of-care genetic analysis (not just *ALK* testing for lung or *KRAS* for colon cancer, etc., but larger panel testing, exome, or other)?” Almost 80% of respondents answered “yes.” The second question was, “If yes, how comfortable do you feel interpreting the genomic information?” The responses to this question were mixed, with approximately 30% saying they were “moderately comfortable,” but approximately 20% were “slightly uncomfortable,” and 25% were “not at all comfortable.”

The results from the second question were broken down into subgroups of types of respondents. Among general oncologists, 25% said they were “slightly uncomfortable,” and 50% said they were “not at all comfortable.” Among Mayo Clinic faculty, approximately 25% were “slightly uncomfortable” and almost 20% were “not at all comfortable.”

The survey further revealed that 70% of respondents “commonly” did not know what to do with genomic results, and more than 80% of respondents would find it helpful to be able to query a genomic tumor board with multidisciplinary expertise regarding a result.

Tumor Board Roles and Challenges

The composition of a multidisciplinary tumor board must be broad and diverse to leverage the widest range of expertise, Dr. McWilliams said. Members of a multidisciplinary team might include, for example, a cytogeneticist who could help to interpret copy numbers and patterns, an anatomic pathologist to help select the best tissue blocks for analysis, and a molecular biologist to help understand potential interactions of molecular pathways, he suggested.

Christine M. Walko, PharmD, BCOP, of Moffitt Cancer Center, added that team members might also include a malignant hematologist and a medical solid tumor oncologist, medical oncology fellows, preclinical and bench scientists, clinical geneticists, bioinformatics experts, clinical pharmacists and specialty pharmacy personnel, and staff from the business or billing office to help with insurance and payment concerns.

With each person bringing his or her own expertise and insight, the tumor board is challenged to identify and interpret information “that can act as a bridge leading from the genetic report to a discussion between the clinician and the patient in the clinic,” Dr. Walko said. Tumor board members give consideration to molecular variants that can provide prognostic information about a patient’s tumor and the potential for response or resistance to specific therapies. They also aid in synthesizing information that may come from a variety of testing platforms and may be presented in different formats. The

board's recommendations must consider the supporting literature behind each variant, the strength of the evidence, and the treatment options that are available and reasonable for the patient based on his or her situation and preferences.

There are challenges to the widespread use of tumor boards, Dr. McWilliams said, one of which is scalability. Much of the work of the tumor board is done on a volunteer or uncompensated basis, and many centers do not have faculty in all of the disciplines needed to fully staff a comprehensive board.

Other challenges include defining what information is clinically actionable and determining what kinds of evidence should be accepted to support the clinical relevance of a particular genetic alteration or response to therapy. Dr. Walko said that more data, and more mature data, are needed, and that increased availability of basket trials will improve enrollment opportunities for patients.

Deep Sequencing and More

D. Neil Hayes, MD, MPH, of the UNC Lineberger Comprehensive Cancer Center, spoke about the use of deep sequencing in cancer care. Although deep sequencing holds great value for research, targeted gene panels may be more appropriate for routine use in clinical cancer care, pending further development and the lowering of costs.

His presentation touched on the role of the tumor board in interpreting sequencing data, as the duties of the panel include identification of functional mutations. Just because a mutation is observed in sequencing data does not mean that it is functional; some mutations in cancer genes are passengers, rather than driver mutations.

Describing the sequencing quality of each assay under consideration is another important function of panel members. Dr. Hayes noted that, although actions for a given patient with a given mutation may be suggested by the tumor board, final treatment decisions may still rest with the oncology provider.

James M. Ford, MD, of Stanford University School of Medicine, spoke about incidental germ-line findings and what to do with them. Sequencing the genome of a patient's tumor or germ line may reveal unexpected information about predispositions to cancer or other diseases. Incidental genomic findings are pathogenic variants that are identified in genomic testing but are not related to the clinical question at hand.

The vast majority of the DNA in a patient's tumor is identical to that in his or her germ line. Therefore, germ-line variants may be found in tumors, including genes for disease or disease risk, genes governing drug responses, and variants of unknown significance. It is important to find out whether patients want this type of information if it is found, especially because its significance may be unclear.

Eliezer Mendel Van Allen, MD, of the Dana-Farber Cancer Institute, spoke about informatics strategies that can be applied to turn sequencing data into patient care. He noted that the number of "data points

per patient" continues to expand, from traditional measures, such as lab results, imaging, and pathology, to the introduction of hotspot genotyping in the previous decade, to targeted panels, to the more recent possibilities of whole-genome sequencing, whole-exome sequencing (WES), and transcriptome sequencing.

One problem with the proliferation of data is how to present it in a form that is usable and understandable to clinicians. Similar to Dr. McWilliams' survey, Dr. Van Allen performed a usability test with a typical cancer genomics clinical report; he showed it to colleagues and found that many had difficulties interpreting the language and presentation of the report.

Several informatics and genomics media have been developed, including My Cancer Genome (mycancergenome.org), MD Anderson Cancer Center's Personalized Cancer Therapy (pct.mdanderson.org), Washington University in St. Louis' Drug Gene Interaction Database (dgidb.genome.wustl.edu), and others. Some of these websites have innovative, interactive interfaces that allow users to click through to more information about genes, variants, available clinical trials, and more.

However, as helpful as these tools may be, more breadth and depth will be needed if clinical WES becomes widely used. Therefore, Dr. Van Allen has been developing the idea of crowdsourcing variant knowledge through a website called TumorPortal (tumorportal.org). Site users can add "community annotations," curating and annotating cancer genomic information to make it more useful for clinical purposes, he said. The hope is that as the entire cancer care community continues to add its insights, this will become a valuable resource that can continue to grow along with the understanding of health and disease.

Watch the session, on the ASCO Virtual Meeting website.