Virtual Molecular Tumor Boards

MOLECULAR TESTING

Resources & Tools for the Multidisciplinary Team

The widespread adoption of molecular biomarker testing and the use of targeted therapies has advanced treatment and improved clinical outcomes in patients with lung and breast cancer. Today, several agents on the market target cancer-specific mutations, including HER2 in breast cancer and EGFR, ALK, ROS1, and BRAF in patients with advanced non-small cell lung cancer (NSCLC), allowing providers to deliver precision cancer therapy. To identify the right targetable mutations, cancer providers must select and perform molecular tests and interpret the results to match patients with appropriate therapies. Even today, the use of molecular tests in clinical practice varies by the type of test and the processes and procedures at individual cancer programs. For example, an analysis of the Flatiron electronic health record (EHR) database revealed wide variations of EGFR testing rates in NSCLC ranging from less than 20 percent up to 100 percent.[1] A recent article published in the *Journal of Oncology Practice* found that 11 percent of oncologists reported having patients with NSCLC who did not undergo ALK testing.[2] Given the growing complexity of the molecular testing landscape, ACCC partnered with the Association for Molecular Pathology (AMP) on a project to help member programs improve how they provide precision cancer care in their own communities.

Kicking Off the Education Project

The ACCC education project, "Virtual Molecular Tumor Boards," examines how innovative formats can help ensure that communication and quality patient care standards are maintained across cancer programs. ACCC introduced this project at the 2016 ACCC National Oncology Conference by hosting a panel discussion with representatives from Seattle Cancer Care Alliance, Washington University in St. Louis, and Frederick Regional Health System. Panelists spoke about leveraging videoconferencing technology to communicate and collaborate on ways to improve molecular testing and patient care in the community (see "Using Virtual Molecular Tumor Boards to Access the Experts," Table 1, page 52).

A virtual molecular tumor board format is especially appealing because it allows participation by a variety of providers across a wide geographic area. Members of multidisciplinary teams from different sites can be invited to join in virtual patient discussions and contribute to treatment plans.[3] Virtual molecular tumor board discussions often lead to recommendations based on targetable genetic alterations.[4]

For this education project, ACCC conducted site visits and group interviews, developing a series of 12 webinars with cancer providers at the following ACCC member programs:

- Seattle Cancer Care Alliance (SCCA)
- University of California Davis (UC Davis)
- Sanford Health
- The Center for Cancer Prevention and Treatment at St. Joseph Hospital (SJO)

ACCC would like to thank the project advisory committee and the members of the cancer teams at these organizations for their guidance, valuable input, and active participation in the Virtual Molecular Tumor Boards project.

Evolving Role of Virtual Molecular Tumor Boards

While the purpose of virtual molecular tumor boards continues to evolve, cancer providers now practice in an era where multiple mutations may be targetable in patients with lung and/or breast cancer; now is a prime time for cancer programs to assess how these tumor boards may enhance care and provide additional support and resources for their providers and patients. Virtual molecular tumor boards can serve several key purposes, including:

- ***Clinical research:*** to identify potential patients who may be eligible for clinical trials.
- ***Continuing education:*** to disseminate education about molecular testing, report interpretations, and actionable results that may impact treatment plans for patients.
- ***Collaboration:*** to bring a team of multidisciplinary providers together to discuss evolving topics, controversial issues, or treatment approaches that are dependent on coordinated care from different members of the team.
- ***Engagement and alignment:*** to ensure that providers across multiple locations are testing and treating patients in a uniform, consistent manner that is based on clinical practice guidelines and the best available evidence.

Virtual molecular tumor boards can be held between a major academic center and a community cancer program. To illustrate this concept, ACCC held a webinar with Seattle Cancer Care Alliance (SCCA) and Summit Cancer Centers on Oct. 26, 2016. During the webinar, Arvind Chaudhry, MD, PhD, (Summit) and V.K. Gadi, MD, PhD, (SCCA) demonstrated how a virtual molecular tumor board could facilitate collaborative discussions on the care of complex patients with breast cancer. They covered a myriad of topics, including molecular testing, assessing for treatment responses, and identifying patients who may be eligible for clinical trials (see "Virtual Molecular Tumor Board Breast Cancer Case Studies," Table 1, page **52**).

As the topic of molecular testing and genomic profiling often refers to complex terms and concepts, ACCC provided an overview of genomic profiling in a Dec. 14, 2016, webinar with Jeffrey Gregg, MD, from UC Davis. Dr. Gregg reviewed genomic alterations found in cancer and explained how mutations, insertions/deletions, fusions, and copy number changes may be targets for drug therapy (see "Overview of Genomic Profiling," Table 1, page **52**).

Ongoing Molecular Testing Issues in Lung Cancer

The landscape of molecular testing in NSCLC has rapidly expanded with the recent approvals of multiple therapies targeting EGFR, ALK, ROS1, and BRAF. Immunotherapy has further advanced the treatment of NSCLC. In 2013, only one targeted agent was approved for ALK+ NSCLC. Today, there are five targeted agents approved for ALK+ NSCLC. There are also three targeted agents approved for EGFR+ NSCLC and a fourth agent approved for patients with EGFR+ NSCLC who have the T790M mutation. In an April 28, 2017, webinar, Melissa Johnson, MD, from Sarah Cannon Research Institute Tennessee Oncology reviewed the evolving landscape of targeted agents for NSCLC. She discussed the latest evidence around agents that target EGFR, ALK, ROS1, and other potentially actionable mutations. Her presentation illustrated how a virtual molecular tumor board could help clinicians in the community learn about ongoing

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Figure 1. SJO Lung Cancer Trials

	Non-Small Cell Lung Cancer					Small Cell Lung Cancer	Rare Diseases or any Lung Patient Failing Treatment
THERAPY	Adjuvant (neoadjuvant genetic testing)	2nd line + squamous	2nd line +	1st line for brain metastasis	Liquid biopsy	Prophylactic cranial irradiation	Targeted therapies (genomic panel testing)
STAGE	Clinical IB-IIIA No neoadjuvant chemotherapy/ radiation therapy Surgical candidate	Stage IV or any stage recurrent (pure squamous) EGFR/ALK negative or not tested	Stage IIIB-IV Failed ≥ 1 lines of systemic therapy, including doublet regimen	Stage IV with central nervous system metastasis	Stage IIIB-IV	Limited or extensive; No central nervous system metastasis; Responding to chemotherapy (English speaking only)	All Stages
TRIAL	**ALCHEMIST**	**LUNG-MAP**	**SERANO** (screening trial, refer to UCI)	**NOVOCURE METIS EF-25**	**BIOCEPT LIQUID BIOPSY**	**NRG-CC003**	**NCI-MATCH**
AGENT	For completely resected adeno: order ALK/EGFR (Central Lab) If ALK+ ALK inhibitor/ Placebo If EGFR+ EGFR inhibitor/ Placebo If adeno ALK/ EGFR- or squamous, test for PDL1. For PDL1+ PD-1 blocking antibody vs. observation after surgery and chemotherapy	Research Order Foundation One 1 Arm Trial Non Match: PD-1 blocking antibody + CTLA-4 blocking antibody svs. PD-1 blocking antibody Match Targets: upcoming	Coming Soon Test for METex 14 Skipping Alteration (archived or fresh) @ Central Lab If positive, refer for treatment with C-MET targeting agent	IT Fields for SRS for 1-10 brain metastases vs. supportive care Excel resected or WBRT Must be receiving therapy for extracranial disease May continue on systemic therapy KPS ≥ 70	Liquid biopsy + tumor tissue to determine molecular marker status for EGFR, ALK, and ROS1	Prophylactic cranial irradiation (PCI) +/- hippocampal avoidance +/- NMDA receptor antagonist use	24 treatment arms for actionable mutations

Source. sjo.org/our-services/the-center-for-cancer-prevention-and-treatment/cancer-programs/thoracic-oncology-program-lung/clinical-trials.

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advances and updates in lung cancer molecular testing and the potential clinical role of emerging agents on the horizon (see "The New Age of Molecular Testing and Targeted Therapies for Lung Cancer," Table 1, page 52).

As additional targeted therapies are approved, the complexity of treating patients with NSCLC is fundamentally revolving around the role of repeat biopsy and repeat molecular testing after patients are started on targeted treatment. Retesting may be necessary to identify potential resistance patterns. The use of liquid biopsy tests (circulating tumor DNA or ctDNA) is one of the latest technologies that has generated a significant level of interest among cancer providers. Cancer programs may need to revisit their own molecular testing policies and procedures to customize them based on the current landscape of available tests, therapies, and the latest clinical evidence. Broad next-generation sequencing (NGS), which is also called comprehensive genomic profiling, is gaining popularity in community settings. As part of the ACCC virtual molecular tumor board webinar series, on Jan. 25, 2017, Jeffrey Gregg, MD, discussed the role of next-generation sequencing for NSCLC. He explained how comprehensive genomic profiling may identify potentially actionable targets in patients with advanced NSCLC who may otherwise have no other treatment options on the horizon (see "Precision Medicine and Personalized Cancer Therapy in Lung Cancer," Table 1, page 52).

The Mar. 13, 2017, ACCC webinar featured the team at St. Joseph Hospital of Orange County (SJO) describing how they have been advancing their molecular testing policies to deliver precision care in their own communities. The team also regularly disseminates information to other clinicians about ongoing clinical trials such as NCI-MATCH, TAPUR, ALCHEMIST, Lung-MAP, and others. As they continue to refine their molecular testing policies, they also align their processes with their clinical research efforts. An example of the SJO Lung Cancer Trials can be seen in Figure 1, left.

Ongoing Molecular Testing Issues in Breast Cancer

Although providers routinely test patients with breast cancer for ER, PR, and HER2, the method of HER2 testing has evolved over the years. This evolution has recently led to some debates regarding optimal testing and interpretation for accurate results. The American Society of Clinical Oncology (ASCO)/College of American Pathologists (CAP) guideline for HER2 testing in breast cancer was originally released in 2007.[5] In 2013, ASCO and CAP updated their guideline to improve the accuracy of HER2 testing to ensure that every eligible patient is identified and treated with HER2 targeted therapies.[6] Sometimes, HER2 results are reported as "equivocal," which means that the test is neither positive nor negative. In such cases, oncologists confer with the pathologist regarding the need for additional HER2 testing on the same or a different tumor sample. While some cancer programs have clear policies and procedures on how to handle equivocal HER2 test results, others leverage tumor boards to discuss some of the latest testing methods and to review guideline recommendations. During a May 4, 2017, ACCC webinar, Michele Carpenter, MD, and David Margileth, MD, from SJO shared their experiences of leveraging their multidisciplinary team to discuss the optimal approach for handling equivocal HER2 test results (see "Challenging Issues in Breast Cancer Management," Table 1, page 52).

Since certain types of breast cancers are linked with hereditary factors, patients often receive genetic testing and counseling. However, hereditary mutations such as BRCA1 and BRCA2 are different from molecular targets such as HER2. Germline (also called hereditary) testing is not the same as somatic mutation testing. To review these issues, Olufunmilayo Olopade, MD, FACP, from the University of Chicago presented a webinar on March 24, 2017, to help clarify the differences between clinical genetics vs. tumor genomic profiling. Clinicians need to clearly understand these differences so that patients are referred for the right types of mutation testing and genetic counseling that may impact their care (see "Clinical Genetics vs. Tumor Genomic Profiling: Relevance in Cancer Care," Table 1, page 52).

Developing a Virtual Molecular Tumor Board Program

ACCC spent time with several member programs to learn how they developed, implemented, and sustained their virtual molecular tumor boards. The ideal program would effectively engage clinicians, maximize meaningful participation, and lead to improved patient care. As ACCC spoke with its members, several key trends and themes emerged, based on different goals and priorities, that led to tailored models for each cancer program.

Trend 1. Clinical Champions

A common theme was the importance of identifying at least one provider who will champion the virtual molecular tumor board effort, influence peers, and demonstrate value in how the tumor board may lead to improved patient care. The champion may be a medical oncologist, pathologist, or surgeon who recognizes the importance of finding potentially targetable mutations in patients with cancer. Other members of the cancer care team, such as advanced practice providers or nurse navigators, may also play a key role in championing virtual molecular tumor boards. Administrative support can enable these champions to overcome institutional barriers around scheduling, time allocation, and resource utilization. Education and outreach tactics must reach providers who work in different locations or specialize in treating specific malignancies.

At UC Davis, pathologist Jeffrey Gregg, MD, plays a key role in developing, organizing, and coordinating its virtual molecular

tumor boards. At Sanford, medical oncologist Steven Powell, MD, serves as a willing clinical champion who effectively engages other members of his team to discuss patient cases and make collaborative treatment decisions that improve patient outcomes. For more see "Engaging Multidisciplinary Clinicians in Genomic Tumor Boards," Table 1, page 52).

Trend 2. Identifying and Preparing Patient Cases

Preparing cases for each virtual molecular tumor board can be time-consuming work, especially if the molecular test results are complex to interpret. Clinical research nurses or nurse navigators can be key to summarizing the patient case, extracting molecular test results, and coordinating the presentation of pathology and radiology findings. Some institutions discuss every patient who undergoes comprehensive genomic profiling at their weekly virtual molecular tumor boards; other cancer programs have rotating schedules that allow different providers to identify and select patients for presentation. Some cancer programs have added a process into their EHRs so that providers can submit a consultative virtual molecular tumor board request for a selected cancer patient.[7] Using a case submission form (Figure 2, right) can help to ensure that the right pathology, radiology, and test results are prepared for the case presentation.

Trend 3. Scheduling Considerations

Cancer programs that are starting a virtual molecular tumor board program may begin with a single monthly meeting. High-volume cancer programs may need to hold weekly virtual molecular tumor boards to allow members of their team to contribute to the care of patients undergoing molecular testing. During a one-hour meeting, it may be possible to hold in-depth discussions around four to six patient cases. Sanford, which began with a single virtual molecular tumor board meeting each week, expanded its schedule to include two weekly meetings that occur at the conclusion of regular tumor boards. When scheduling virtual molecular tumor boards, consider the time zones of the remote participants. When SCCA engaged in a virtual molecular tumor board project, the schedule had to take into account network sites across three different time zones.

Trend 4. Access to Genomic Experts

Many cancer programs employ genetic counselors to speak with patients about hereditary genetic risks. However, the interpretation of comprehensive genomic profiling reports requires the skill of bioinformatics specialists, molecular pathologists, and other genomic experts. Community cancer programs may consider developing collaborations and partnerships with academic organizations or other institutions that provide this level of consultative expertise. Some lab testing companies allow their molecular pathologists and bioinformatics specialists to participate in virtual molecular tumor board discussions. These individuals provide test interpretation services, but do not provide clinical treatment advice. UC Davis conducts its virtual molecular tumor board in partnership with Foundation Medicine to gain access to genomic experts who have seen a wide variety of unusual mutations in cancer patients. Virtual molecular tumor board discussions can be an effective way to identify patients who may be candidates for clinical trials. Some molecular testing companies include clinical trial matching information in the test results. Commercial companies like N-of-One offer clinical interpretation and trial matching services. The American College of Medical Genetics and Genomics (ACMG) and the Association for Molecular Pathology (AMP) are national organizations that train and equip genomic experts in cancer. For more see "The Role of Genetics Professionals in a Community Cancer Program," Table 1, page 52.

Trend 5. Role of Technology

The use of secure video conferencing technology platforms lets remote participants engage in rich clinical discussions about treatment plans. These platforms allow providers and researchers to participate in discussions while they are off-site. The use of multiple screens and monitors in the tumor board conference room also allows pathology, radiology, and other disciplines to seamlessly present their findings. Technology platforms can enable remote participants to toggle screens and follow the discussions. At Sanford, the team has developed a progress note template to summarize the discussions from their virtual molecular tumor boards. This template allows providers to easily review the information as they are developing treatment plans and coordinating follow-up care. Be sure to obtain legal and regulatory review around potential issues that may impact patient privacy and liability.

Trend 6. Participation and Engagement

The effective use of virtual molecular tumor boards ultimately provides more patient-centered care. Clinicians, particularly medical oncologists and nurses, are most likely to directly experience this value with their own patients. As a result, they may be naturally inclined to actively participate in virtual molecular tumor boards and even emerge as potential champions. Other clinicians, such as surgeons, radiologists, pathologists, and pulmonologists, may need additional motivation to keep them engaged. These essential members of the cancer care team play a critical and active role in virtual molecular tumor board discussions that impact treatment plans for patients. At Sanford, the cancer center provides free lunch and CME credits at every virtual molecular tumor board. Cancer programs that employ physicians may choose to track participation at virtual molecular tumor boards and link a portion of physician compensation to their attendance. For more, see

"Real-World Considerations When Implementing a Genomic Tumor Board Program," Table 1, page 52.

Looking to the Future

As the term "precision medicine" becomes more ubiquitous in cancer care delivery, the role of molecular testing is increasingly an integral part of shaping personalized treatment decisions and care plans. Cancer therapy that is driven by genomic testing can lead to more personalized treatment approaches that improve clinical outcomes.[8] The growing complexity of molecular testing and interpretation presents both a challenge and an opportunity for community cancer programs to develop collaborative approaches that effectively engage teams of clinicians to care for patients. Furthermore, implementing newer cancer treatments, such as immunotherapy, may require testing for PD1/PD-L1 and other biomarkers. Before starting a virtual molecular tumor board, cancer programs must clearly define the metrics for success and perform a baseline assessment prior to launch. In the rapidly evolving era of precision medicine, clear communication between members of the multidisciplinary team is essential in providing optimal patient care. An effective virtual molecular tumor board can be a valuable care collaboration tool that improves knowledge, elevates care delivery, and ultimately improves outcomes in cancer patients. OI

Figure 2. An Example of a Case Submission Form

Tumor Board _____

Date Submitted _____

Patient Name _____ E# _____

Presenting Physician _____

Data to Review

- ☐ Pathology
- ☐ Imaging
- ☐ Nuclear medicine
- ☐ Other _____

Dates

_____

_____

_____

_____

Clinical Focus

New patient/new presentation (full review) _____

Specific clinical focus area _____

Surveillance/interval evaluation _____

** Case brief submitted by 12:00 noon on the day prior to the conference.

Source. Sanford Health

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Table 1. Virtual Molecular Tumor Boards: An ACCC Educational Series

ACCC partnered with the Association for Molecular Pathology to host 12 educational webinars that utilize case-based lessons surrounding molecular testing for breast and lung cancer. Featuring experts from these leading cancer programs: Seattle Cancer Care Alliance, University of California Davis, Sanford Health, and St. Joseph Hospital of Orange, The Center for Cancer Prevention and Treatment, the webinars listed below can be accessed online at: accc-cancer.org/resources/virtual-tumor-boards.asp.

1.	Using Virtual Molecular Tumor Boards to Access the Experts
2.	Virtual Molecular Tumor Board: Breast Cancer Case Studies
3.	Overview of Genomic Profiling
4.	Precision Medicine and Personalized Cancer Therapy in Lung Cancer
5.	An Ongoing Journey to Advance Molecular Testing in Lung Cancer
6.	The Role of Genetics Professionals in a Community Cancer Program
7.	Clinical Genetics vs. Tumor Genomic Profiling: Relevance in Cancer Care
8.	The New Age of Molecular Testing and Targeted Therapies for Lung Cancer
9.	Challenging Issues in Breast Cancer Management
10.	Engaging Multidisciplinary Clinicians in Genomic Tumor Boards
11.	Real-World Considerations When Implementing a Genomic Tumor Board Program
12.	Key Concepts and Future Directions in Molecular Testing and Care Delivery