

## Multidisciplinary Molecular Tumor Boards: Two Models

In October 2018, the Association of Community Cancer Centers (ACCC) hosted a pre-conference workshop at its 35th National Oncology Conference. Sessions focused on models which show how oncology pharmacists can best respond to rapid changes occurring in the oncology environment, including the emergence of molecular tumor boards. Molecular tumor boards offer a vital resource to support delivery of precision medicine to oncology patients. Various members of the cancer care team should be represented, including the oncology pharmacist.

### Personalized Medicine and Next Generation Sequencing

Next generation sequencing (NGS) is becoming increasingly important for diagnosing cancer, predicting prognosis, and guiding personalized treatment for patients. In 2006, Moffitt Cancer Center in Tampa, Florida, launched Total Cancer Care™ (TCC). TCC is a unique research study which entails collecting tumor specimens and clinical data, including NGS results, throughout the lifetime of patients to create evidence in support of precision medicine.<sup>1</sup> As a result, a multidisciplinary, team-based service has evolved at Moffitt to help translate this personalized cancer care approach from research into clinical practice. In addition to pharmacists, the team includes members from pathology, medical genetics, bioinformatics, translational research, laboratory science, social work, oncology and hematology physicians and nurses, and patient representatives. Todd Knepper, PharmD, Personalized Medicine Specialist, Department of Individualized Cancer Management at the Moffitt Cancer Center provided an overview of this clinical service and the in-house and external vendor NGS panels used to test tumors for somatic mutations.

Reporting for these panels is typically patient-specific and comprehensive, although there is considerable variation in the format and content of reporting NGS results. At Moffitt, rather than leave the interpretation of NGS panel results to physicians, the molecular tumor board (MTB) offers a clinical service that reviews in-house and commercial NGS panel results on a daily basis. The Personalized Medicine Clinical Service and Clinical Genomics Action Committee (CGAC) are pharmacist-led clinical programs at Moffitt Cancer Center that meet weekly to discuss the NGS results and recommend treatment options including the potential for clinical trial enrollment.<sup>2</sup> Pharmacists on the team serve as attendings on the Personalized Medicine Clinical Service and are responsible for reviewing and

interpreting NGS results, leading the MTB meetings, and documenting MTB outcomes in the electronic health record. In addition to reviewing off-label data, pursuing tiered therapy authorizations, and considering drug-drug interactions to support the treating physician, the pharmacists assist in the procurement of off-label therapies.

This Personalized Clinical Medicine Service is supported by a (CGAC) dashboard that reports results and potential clinical implications (Figure 1).

### The Impact on Patients of the MTB

Cory Vela, PharmD, BCOP, is a Clinical Pharmacy Specialist, Precision Medicine at the University of Kentucky (UK), Markey Cancer Center. His responsibilities as a pharmacist participating in the UK MTB include gathering and interpreting all patient-specific molecular alteration data; outlining potential targeted therapy (on-label, off-label, clinical trial) options based upon molecular alterations identified, prior treatment history, or persistent toxicity from prior therapy; facilitating treatment-oriented discussion during the UK MTB; and presenting, or recruiting other MTB members to present primary literature to the UK MTB to support targeted therapy recommendations.

Patients who pursue clinical trials at UK are treated in the Precision Medicine Clinic in which Dr. Vela is the clinical pharmacist. During these visits Dr. Vela obtains a medication history, discusses treatment calendars, addresses drug-drug interactions, explains the mechanism of action of selected targeted therapy, outlines potential treatment-related toxicities, and follows the patient to assist in toxicity management. Occasionally, Dr. Vela may meet with the patient to discuss UK MTB recommendations and explain the rationale behind recommended treatment plans. He also works with UK Specialty Pharmacy Services to aid with prior authorization processes and financial considerations.

Dr. Vela provided an overview of the MTB process at UK (Figure 2),<sup>3</sup> and the impact of MTB decisions on patients.

UK physicians, and those at affiliate institutions in the state of Kentucky, can order a range of tests (e.g., hotspot mutational testing, limited polymerase chain reaction (PCR) gene panel, immunohistochemistry (IHC), NGS panels), but in contrast to the Moffitt model, the UK MTB does not review all reports. Rather, physicians

**Figure 1. Clinical Genomics Action Committee Dashboard**

### 1. Basic Mutation Information

#### Gene Information

ALIAS	B-RAF1 BRAF1 NB7 RAFB1
DESCRIPTION	v-raf murine sarcoma viral oncogene homolog B

#### Mutation Site Information

### 2. Mutation Frequency in 1000 Genome Project

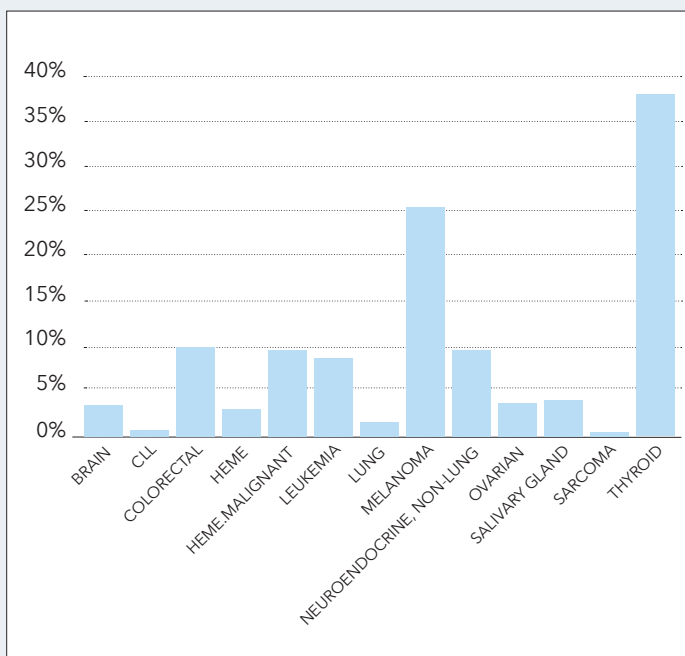
This mutation site is not in 1000 Genome Project.

### 3. Mutation Frequency over CGAC Samples

Across Different Tissue Types Search Table:

CANCER TYPE	PROTEIN	SAMPLE WITH MUTATION	TOTAL SAMPLE	FREQUENCY (%)
	V600E	1	50	2
Brain	V600E	14	423	3.3097
CLL	V600E	4	605	0.6612
Colorectal	V600E	20	212	9.434
Heme	V600E	1	35	2.8571
Heme.malignant	V600E	1	11	9.0909
Leukemia	V600E	5	60	8.3333
Lung	V600E	12	774	1.5504
Melanoma	V600E	82	216	24.186
Neuroendocrine non-lung	V600E	1	11	9.0909
Ovarian	V600E	1	28	3.5714
Salivary Gland	V600E	1	26	3.8462
Sarcoma	V600E	1	204	0.4502
Thyroid	V600E	13	36	36.1111

Mutation Frequency of BRAF (V600E)



VIEW/SAVE PLOT IMAGE

### 4. ClinVar: Clinical Significance

No information for this mutation site in ClinVar.

### 5. Align-GVGD grade

No Align-GVGD information.

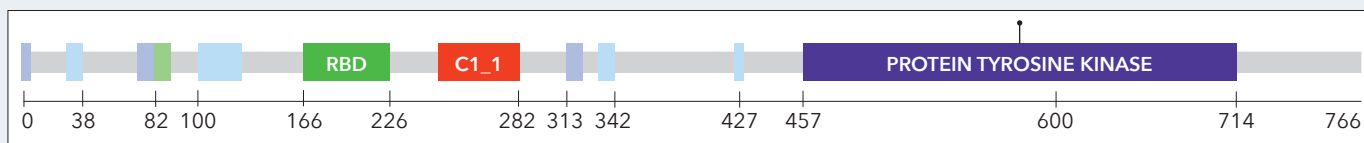
### 6. IARC TP53 Database Information

No information for this mutation site in IARC TP53 Database.

### 7. EVS Information

No information for this mutation site in EVS Database.

### 8. Mutation in Functional Domain



**What is the best time to use NGS testing, which patients should we be testing, and what could we do to improve the testing process?**

Typically, physicians order an NGS panel when they know a patient is a candidate for additional therapy. The best timing for testing is a difficult question to answer; however, Dr. Vela noted that testing at diagnosis is optimal and FDA approved for many cancers (e.g., lung). In other cancer types, test timing is less clear cut. Some baseline mutations are associated with genetic shift and can change over time from primary therapy to relapse depending on the kind of therapy patients have received. In addition, given the costs of testing and potential for off-label therapies, especially in later lines of therapy, some commercial testing companies have started to request pre-test evidence of utility to justify potential cost. Current best practice involves discussion between patients and their providers, and providers' discussion with members of the MTB, prior to ordering mutational testing.

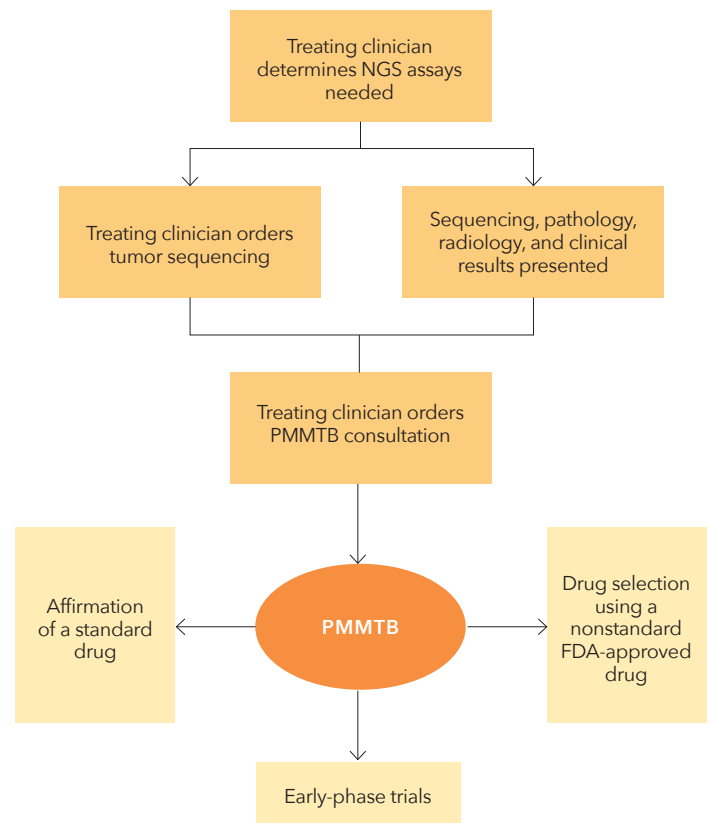
in all participating sites can request for the UK MTB to review a patient's molecular data results via EMR. The MTB meets twice a month, with cases reviewed by physicians, radiologists, pathologists, researchers, and pharmacists. The interdisciplinary members present pertinent patient history, response to prior therapy, pathologic review of current and/or prior biopsies, and mutation panel results to try to identify potential patient-specific therapeutic options (e.g., standard of care, clinical trials, or off-label therapy). Following MTB discussion, recommendations and supporting literature are presented to the treating physician and documented in the electronic medical record (EMR).

In a previous retrospective study of Moffitt patients, Drs. Vela, Knepper, and colleagues reviewed the CGAC database for solid tumor patients and reported that lung cancer was the most common tumor type for which molecular testing was ordered, followed by brain and colorectal cancer. The retrospective analysis identified that 16.3% (n=175) of patients were eligible for on- or off-label therapy based upon 17 potentially actionable mutations.<sup>3</sup> Dr. Vela suggested that perhaps the number of patients eligible for targeted therapy would have been greater if clinical trial eligibility had been assessed or if a larger number of genes was evaluated.

**Pre-Empting Financial Toxicity: The Role of Financial Advocates in the MTB**

Financial toxicity is increasingly common among patients receiving cancer treatment; therefore, treatment cost estimates are often discussed at MTBs and molecular testing information is included in pre-authorization documentation. Clara Lambert, BBA, OPN-CG, Oncology Financial Navigator at Advocate Good Samaritan Bhorade Cancer Center, presented an overview of how financial advocates (e.g., patient/financial navigators, social workers, nurses) can represent patients' financial concerns in the MTB setting and how their advocacy role is evolving. Financial advocates represent the patient voice at the MTB. Ms. Lambert noted, "I have found that if the patient has already expressed financial concerns to me, and the tumor board is discussing options in treatment, that I need to speak up and let them know of the concerns, and the potential costs of the treatments they are considering. When I make this statement, I also make sure that I know what available assistance the patient can qualify for. Ultimately, it is up to the physician and the patient to determine the best treatment, but I do think that both need to do this with all of the information available to include efficacy, side effects, cost, and assistance available."

**Figure 2. Precision Medicine Molecular Tumor Board (PMMTB) Flow Diagram**



Source: Walko C, Kiel PJ, Kolesar J. Precision medicine in oncology: new practice models and roles for oncology pharmacists. *Am J Health Syst Pharm.* 2016;73(23):1935-1942.

## Who explains the financial implications of treatment to patients?

Financial advocates can help patients understand insurance coverage, what their plan is likely to cover, and what the potential out-of-pocket costs are likely to be. To avoid treatment delays, oncology financial navigator Lambert also advises advocates to gather as much complete information as possible up front to submit to payers, including NGS testing results, and treatment regimen(s), including dosages. It is important to explain to patients the rationale for including this information in authorization submissions and to keep them in an ongoing communication loop. Sometimes patient responses are non-verbal and signal extreme anxiety. Lambert finds it instructive to watch a patient's body language and to acknowledge there are instances where a social work referral might be great.

In order to represent patient concerns and support access to recommended treatment, financial advocates need to be familiar with compendia (e.g., Micromedex, Lexicomp, National Comprehensive Cancer Network) and patient insurance coverage and understand how the treatment plan will work with the patient's insurance (e.g., not only on-label, but also off-label, clinical trial enrollment, and multi-year treatment). Financial navigation software tools can be invaluable in streamlining and automating financial processes, identifying patients at financial risk, and suggesting personalized funding opportunities.

Financial advocates work alongside oncology pharmacists to ensure selected therapy is affordable/available prior to treatment initiation. Advocates will work with both on- and offsite specialty pharmacy representatives and continue to provide financial navigation assistance to ensure continuity for patients. Several portals allow advocates to monitor the prescription, financial assistance status, and the authorization process and determine when it might be necessary to find new assistance funds and patient support services.

This in-depth knowledge is key in treatment planning discussions, especially as NGS panels often report off-label therapies as potential treatment outside of guidelines/compendia. Ms. Lambert noted that in the case of combination treatment that involves off-label therapy, pre-emptive navigation is prudent to identify free medication prior to treatment initiation. She also emphasized that financial advocates should establish regular communication with patients throughout the treatment planning and delivery process to keep them apprised of insurance coverage and funding assistance. Financial advocates can help to alleviate patient anxiety through regular communication about the authorization, denials, and appeals processes. ■

## References

- 1 Fenstermacher DA, Wenham RM, Rollison DE, Dalton WS. Implementing personalized medicine in a cancer center. *Cancer J*. 2011; Nov-Dec 17(6):528-36.
- 2 Knepper TC, Bell GC, Hicks JK, et al. Key lessons learned from Moffitt's molecular tumor board: The Clinical Genomics Action Committee Experience. *Oncologist*. 2017;22(2):144-151.
- 3 Vela CM, Knepper TC, Gillis NK, et al. Quantitation of targetable somatic mutations among patients evaluated by a personalized medicine clinical service: Considerations for off-label drug use. *Pharmacotherapy*. 2017;37(9):1043-1051.

The **Association of Community Cancer Centers (ACCC)** is the leading education and advocacy organization for the cancer care community. ACCC is a powerful network of 25,000 cancer care professionals from 2,100 hospitals and practices nationwide. ACCC is recognized as the premier provider of resources for the entire oncology care team. For more information, visit [acc-cancer.org](http://acc-cancer.org) or call 301.984.9496. Follow us on Facebook, Twitter, and LinkedIn, and read our blog, ACCCBuzz.

The **ACCC Oncology Pharmacy Education Network** advocates on behalf of hematology/oncology pharmacists as vital members of the cancer care team, and is committed to developing educational resources and multidisciplinary connections that advance the field and elevate oncology pharmacy professionals to top-of-license practice.



Association of Community Cancer Centers