Put It on the Board

Broad-based molecular testing for NSCLC

September 2018—A recently published study on broad-based genomic sequencing and survival among patients with advanced non-small cell lung cancer in the community oncology setting should not lead to the conclusion that such sequencing should be avoided in nonsquamous NSCLC, say Paul A. Bunn Jr., MD, and Dara L. Aisner, MD, PhD, of the University of Colorado Denver, Aurora.

Dr. Bunn, of the Department of Medical Oncology, and Dr. Aisner, of the Department of Pathology, in an editorial published Aug. 7 in *JAMA* (320[5]:445–446), caution readers about the study published in the same issue, which found that broad-based sequencing (more than 30 cancer genes) directly informed treatment in a minority of patients and was not independently associated with better survival (Presley CJ, et al. *JAMA.* 2018;320[5]:469–477).

The study of 5,688 patients with advanced NSCLC was based on data acquired through abstraction and aggregation of information from the electronic medical record from 191 U.S. community oncology practices. The results indicate that "broad-based genomic sequencing identified at least 125 patients with alterations in *ROS1, MET, BRAF, ERBB2, NTRK1-3,* and *RET*," Drs. Bunn and Aisner write, "yet only 36 patients received a broad-based genomic sequencing informed therapy." They say that identifying but not treating molecular drivers would not improve survival as demonstrated in a study published in 2014 (Kris MG, et al. *JAMA.* 2014;311[19]:1998–2006).

"This gap between finding and treating molecular alterations in the community-based clinical setting highlights the reality that obtaining more tumor genomic information must be complemented with clinician education and decision support to understand the importance of matched therapy, and demonstrates a strength of harnessing EMR data to identify potential gaps in practice," they write.

Drs. Bunn and Aisner advise caution about the study, which they say provides important insights into how broad-based sequencing is used in the community oncology setting, for other reasons:

- Progression-free survival, objective response rates, and quality of life can be improved with specific TKIs used in first-line therapy, but these outcome measures were not assessed in the EMR-based study, which relied solely on survival as the end point.
- The 2011–2016 time frame of the study "almost entirely predated the routine and FDA-approved use of TKIs for *ROS1* rearrangements and *BRAF* V600E mutations, and included the period immediately following FDA approval of targeted therapy for *ALK* rearrangements."
- "Some of the differences in alterations identified but not treated may have been related to the availability of new therapies, resulting in a potential study bias against broad-based genomic sequencing."
- "[T]he incremental value of a cutoff of 30 genes analyzed may place the bar too high to appreciate a survival

advantage," Drs. Bunn and Aisner write, "and the tissue, time, and cost savings due to next-generation sequencing were not considered."

AMP report: DNA variants in chronic myeloid neoplasms

The Association for Molecular Pathology published consensus, evidence-based recommendations for managing most chronic myeloid neoplasms and developing high-throughput pan-myeloid sequencing testing panels. The report was released Aug. 20 online in the *Journal of Molecular Diagnostics* (doi:10.1016/j.jmoldx.2018.07.002).

The biological complexity and multiple forms of CMNs have led to variability in the genes included on the available panels. The AMP CMN Working Group was established to review published literature, summarize key findings that support clinical utility, and define a minimum set of critical gene inclusions for all high-throughput pan-myeloid sequencing testing panels.

The AMP CMN Working Group proposed the following 34 genes as a minimum recommended testing list: *ASXL1, BCOR, BCORL1, CALR, CBL, CEBPA, CSF3R, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NF1, NPM1, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1,* and *ZRSR2*.

"While the goal of the study was to distill the literature for molecular pathologists, in doing so we also revealed recurrent mutational patterns of clonal evolution that will aid hematologist/oncologists, researchers, and pathologists in understanding how to interpret the results of these panels as they reveal critical biology of the neoplasms," Annette S. Kim, MD, PhD, associate professor of pathology at Harvard Medical School and Brigham and Women's Hospital, said in a statement. She is the AMP hematopathology subdivision chair and CMN Working Group chair.

Cervical cancer screening guidelines recommend HPV testing alone

The U.S. Preventive Services Task Force issued cervical cancer screening guidelines that recommend, for the first time, HPV testing alone as the first-line screening test to detect cervical cancer and precancer.

The USPSTF statement, published Aug. 21 in *JAMA*, assigns a grade of "A"—indicating the service is recommended and there is a "high certainty that the net benefit is substantial"—for high-risk HPV testing every five years for women 30 to 65. It also retains prior recommendations for Pap testing alone every three years for women 21 to 65 and cotesting (Pap plus HPV) for women 30 to 65. The cotesting option is one the CAP advised be retained, in comments submitted last fall to the USPSTF. The CAP had also advised primary HPV screening every three years, not five.

Sysmex opens new Center for Learning

Sysmex opened in August its new 98,000-square-foot Center for Learning in Vernon Hills, Ill.

Inside Sysmex's new Center for Learning, from which instructors

broadcast live training classes on how to use the company's diagnostic devices.

The new space has more than triple the training capacity of Sysmex's previous Center for Learning. It has the capacity to train up to 4,400 people per year, including 3,000 customers, virtually and on site, and 1,400 Sysmex employees. The center houses seven broadcast studios for virtual instructor-led training.

DCISionRT study finds prognostic, predictive power

PreludeDx announced the results of a large cross-validation study of its DCISionRT test in patients with ductal carcinoma in situ that found DCISionRT to be a strong predictor of radiation benefit and able to identify patients with elevated recurrence risk who would be considered low risk by traditional clinical assessment.

The study report, titled "A biologic signature for breast ductal carcinoma in situ to predict radiation therapy (RT) benefit and assess recurrence risk," is available online in *Clinical Cancer Research* (doi:10.1158/1078-0432.CCR-18-0842).

Lead investigator Fredrik Wärnberg, MD, PhD, associate professor of surgery at Uppsala University and a member of the Swedish Breast Cancer Group, said in a Prelude-issued statement: "The study analyzed the biology and clinical factors of 526 patients using DCISionRT and demonstrated that the biologic signature was excellent at identifying which patients would have a DCIS or invasive breast cancer recurrence within 10 years, but—importantly—also distinguished the patients most likely to have clinically meaningful radiation therapy benefit from those that would not."

The DCISionRT Score identified patients with 10-year invasive breast cancer risks from three percent to 40 percent with surgery alone, or three percent to 10 percent with surgery and radiation therapy. The study also showed that DCISionRT distinguishes risk independent of clinicopathologic factors, according to Prelude, where the test found that 42 percent of clinicopathologically low-risk patients were in the DCISionRT elevated risk group and had a 10-year total recurrence risk of 31 percent.

In an oral presentation at the December 2017 San Antonio Breast Cancer Symposium, Dr. Wärnberg presented predictive data from the SweDCIS trial that demonstrated that the DCISionRT test was able to accurately stratify patients into a low-risk group with a non-significant risk reduction of one percent from radiation therapy and an elevated risk group that received a significant nine percent absolute benefit from radiation therapy.

Agena, PerkinElmer to collaborate

Agena Bioscience has entered into a collaboration with PerkinElmer in which the LabChip GX Touch nucleic acid analyzer for quality assessment and quantitation of DNA will be incorporated into the upfront workflow of Agena's MassArray system. The companies have focused on targeting ctDNA in oncology liquid biopsy, where they say the combined systems support a single-day sample to results workflow for laboratories.

PerkinElmer's LabChip GX Touch nucleic acid analyzer provides electrophoretic visual quality assessment and quantitation down to 25 pg/µL for DNA with flexible sample throughput options including 96-well and 384-well. According to Agena, this provides a streamlined upfront process to its 96- and 384-chip systems and the UltraSeek chemistry for liquid biopsy.

Agena says that, in evaluations performed by its team, the LabChip system ensured that sufficient DNA was present in the sample to achieve the sensitivity capabilities of the UltraSeek chemistry while efficiently identifying samples compromised by preanalytical variables that could result in false-negative results.