G2 INTELLIGENCE
A DIVISION OF PLAIN LANGUAGE MEDIA

DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

March 2017

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Discordant Commercial, Next-Gen Tumor Profiling Results May be Clinically Relevant

Next-generation sequencing is increasingly becoming commonplace to match cancer-associated alterations with targeted treatments. But, a new study raises concerns that marked differences in results between two commercially available genetic tests for oncology patients may be "clinically relevant."

The research letter, published recently in *JAMA Oncology*, compared the tissue-based FoundationOne test (F1; Foundation Medicine) with the blood-based Guardant360 (G360; Guardant Health) test. F1 characterizes the exons of 315 cancer-associated genes and introns from 28 genes involved in rearrangements, while G360 sequences 70 genes from cell-free circulating DNA. Previous published studies have shown that both the F1 and G360 tests have high specificities (above 99 percent), but lower sensitivities.

The present study compared results from both tests in nine patients seen at a community oncology practice. The level of concordance between the platforms was compared among the two men and seven

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Many Breast Cancer Patients Not Referred for Genetic Testing; Genetic Counseling Needed

Physicians often fail to recommend genetic testing for breast cancer patients at high risk for mutations, according to a research letter published Feb. 7 in the *Journal of the American Medical Association*. The findings, the authors say, indicate both the need to improve physicians' assessments of patients' risk and need for genetic testing, as well as the need to expand the availability of genetic counseling.

"The fact that many women are not offered genetic testing after a diagnosis of breast cancer is an important illustration of the challenges of driving advances in precision medicine into the exam room," says co-senior author Steven Katz, M.D., from University of Michigan, in a statement.

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Discordant Commercial, Next-Gen Tumor Profiling Results May be Clinically Relevant, *from page 1*

women (mean age, 61 years). Testing occurred from April 14, 2015 to Jan. 30, 2016. In addition to comparing identified genomic alterations, test results were compared regarding recommended drugs.

The researchers found one patient had no identified genetic alterations using either test. Among the remaining eight patients, 45 alterations were identified, but only 10 alterations (22 percent) were concordant between the platforms. For two of the eight patients, there was no concordance among the reported alterations. Alterations that are unique to F1 test, which detects a "much broader range" of aberrations than G360, were excluded from analysis. Concordance improved "only slightly" to 28 percent (5 of 18 alterations) when comparisons were limited to variant allele frequencies of 1 percent or greater.

For the eight patients with identified alterations, 36 drugs were recommended, in total. However, only one-quarter of the drugs were recommended for the same patients by both platforms. In five patients there was no overlap between the drugs recommended by the two tests. Concordance among recommended drugs improved to 62 percent (8 of 13 drugs), when reported mutations were also concordant.

In seeking an explanation for the discordant test results, the authors cite differences in timing between the two tests as a possible source, but note that seven of the eight patients with reported alterations underwent both tests within a 2.5-month period. Other potential sources of the discordance are tumor heterogeneity and differences in the variant-interpretation process.

"Since both the F1 and the G360 tests are performed in thousands of patients with cancer each year, these findings are clinically relevant," write the authors led by Nicole M. Kuderer, M.D., from University of Washington, Seattle. "In-depth comparisons of next-generation sequencing tests across larger numbers of patients with cancer are needed to improve concordance and clinical utility."

The authors note that theirs was not the first to identify "significant discordance." Two studies comparing tissue-based next-generation sequencing tests and another report also comparing the F1 and G360 tests, all found discordant test results.

Takeaway: Initial comparisons of commercially available next-generation sequencing tests to identify cancer-related variants targetable by therapies, raise concerns regarding the potential clinical relevance of discordant genetic findings and resulting drug recommendations.

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Diagnostic Testing and Emerging Technologies
(ISSN 2330-5177) is published by G2 Intelligence, Plain Language Media, LLLP, 15 Shaw Street, New London, CT, 06320.
Phone: 1-888-729-2315
Fax: 1-855-649-1623
Web site: www.G2Intelligence.com.

FDA Reclassifies Rapid Flu Antigen Tests

Effective mid-February the U.S. Food and Drug Administration (FDA) reclassified antigen-based, rapid influenza virus antigen detection test systems (RIDTs) used directly on clinical specimens from Class I to Class II devices. Further, the FDA introduced special controls aimed at improving the overall quality of flu testing and reducing the number of misdiagnosed cases.

Given that misdiagnosis of the flu could lead to inappropriate use of antibiotics, failure to use antiviral therapy, and ineffective infection control measures, the FDA believes premarket notification is necessary for these tests "to provide reasonable assurance of safety and effectiveness."

RIDTs are widely used in non-clinical laboratory settings, such as physicians' offices, and evidence from the U.S. Centers for Disease Control and Prevention and the Association of Public Health Laboratories showed the tests were performing poorly in medical practice, resulting in many misdiagnosed cases.

In addition to the reclassification, special controls were established to mitigate health risks. These special controls include new minimum performance criteria; use of FDA-accepted comparator method for establishing the performance (presently, either an FDA-cleared nucleic acid-based test or a correctly performed viral culture method); and annual analytical testing of circulating strains, based on the CDC's annual standardized seasonal influenza virus test panel, as well as emergency analytical reactivity testing of newly emerging strains, when needed.

Additionally, the FDA's final order requires that the results of the last three years of annual analytical reactivity testing be included as part of the device's labeling. The FDA is giving manufacturers one year to come into compliance with the final rule.

Takeaway: Manufacturers have one year to come into compliance with new FDA regulations of RIDTs, including reclassification and implementation of special controls.

Dx Investments Hold Steady in 2016, Number of Exits Declines

Investments in the diagnostics and tools (Dx/Tools) sector remained steady in 2016, according to Silicon Valley Bank's annual report, *Trends in Healthcare Investments and Exits 2017*. The report authors found the industry is attracting new investors and is optimistic that the sector's prospects for big exits (valued at $50 million or more) will improve in 2017.

Silicon Valley Bank (SVB) says that overall health care venture investing was "strong" in 2016, but did not reach the record levels set in 2015. However, in 2016, Series A investments in early-stage technologies set records in all health care sectors, including Dx/Tools.

SVB data shows that the Dx/Tools sector saw "meaningful" early-stage momentum last year, with 51 deals closing in 2016, the highest number of deals since the 39 that closed in 2013. The value of these deals rose to a high

"While Dx exits declined in 2016, we see a significant number of companies ramping revenue towards $30-$50 million."

— Jonathan Norris
Managing Director,
Silicon Valley Bank

of $478 million, the highest since 2014's $252 million in series A investment. Within the sector Dx outpaced tools garnering 59 percent of the Series A dollars invested. Grail was the largest venture-backed Dx/Tools Series A deal ($125 million) seen.

Encouragingly, the most active investors in the device and Dx/Tools sectors grew more diverse (e.g., corporate venture, angel groups, incubators and accelerators, and private equity). Tech-focused venture capitalists became "very active" in Dx/Tools, with Data Collective (San Francisco) leading investors with eight active Dx/Tools deals in 2015-2016. These investments follow the trend of increasing use of big data and bioinformatics within the Dx/Tools sector. LabCorp and Illumina emerged as active corporate venture investors with three and two active deals in the Dx/Tools space in 2015-2016.

Geographically, California remains the most active region for new investment in Dx/Tools with 19 deals in Northern California (valued at 1.193 billion) and seven deals in Southern California (valued at $345 million). Massachusetts was the second most active state for new investments in the Dx/Tools space with seven deals valued at $106 million.

Overall, for the health care industry, a slower pace of initial public offerings (IPOs) led to lower distributions in 2016. As a sector, though, Dx/Tools companies struggled to reach big exits and had no IPO activity. SVB analysts say, though, that "large investment bets" have been made in advancements in bioinformatics, potentially "setting the stage" for more big exits in the coming years. In addition to big data, SVB analysts are watching companies with new tools to enable drug development and high-end sequencing, as well as those working to make diagnostics less invasive (e.g., liquid biopsies).

"While Dx exits declined in 2016, we see a significant number of companies ramping revenue towards $30-$50 million," writes the report's lead author, Jonathan Norris, managing director at Silicon Valley Bank (Santa Clara, Calif.). "We think that level should attract acquirer interest."

In 2016, the Dx/Tools sector had just four mergers and acquisitions (M&As) and no IPOs, compared to eight M&As and five IPOs in 2015. Of the four big exits (deals valued at $50 million or more) in 2016, three were in the tools space and only one was a diagnostics deal. Despite the low number of deals, the total deal value went up ($175 million in 2016 versus $164 million in 2015), while the median years to exit (from the time of the close of its first institutional round of financing) increased in the Dx/Tools space to 7.7 years.

While the IPO market was slow overall, the Dx/Tools sector may have been particularly hampered by the "poor" after-market performance of previous IPOs. SVB says all five 2015 Dx/Tools IPOs are trading below their IPO prices.

Takeaway: Experts are not expecting large swings in investment in the Dx/Tools sector during 2017, although they are optimistic that M&A activity will pick up in 2017.

Testing Guidelines *at a Glance*

New Definition for Abnormal Liver Chemistry

For the first time, the American College of Gastroenterology issued a practice guideline to define a healthy serum alanine aminotransferase (ALT) level. 'Normal' ALT (19 to 25IU/L for females 29 to 33 IU/L for males) is based on multiple studies correlating elevated ALT levels and liver-related mortality in populations worldwide. ALT levels above 25 IU/L in women and above 33 IU/L in men should be assessed by physicians.

"With the broad range of 'upper limit of normal' levels for ALT that vary from institution to institution, clinicians may not think to evaluate an ALT level of 70 IU/L, as this may be within the normal level for the reporting laboratory—even though this level of elevation is associated with increased liver-related mortality," explains guideline co-author Paul Y. Kwo, M.D., from Stanford University, in a statement. Additionally, the guidelines provide clinicians a step-by-step framework for the evaluation of elevated ALT.

Molecular Biomarkers for Colorectal Cancer

A joint guideline from the American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and American Society of Clinical Oncology, published in the March issue of the Journal of Molecular Diagnostics establishes evidence-based recommendations for mutational testing of EGFR signaling pathways for patients with colorectal cancer (CRC), as well as key steps laboratories can take to operationalize CRC molecular testing.

A systematic literature review found evidence supporting mutational testing to guide therapy of CRC with anti-EGFR monoclonal antibodies. Mutations in BRAF and MMR have "clear prognostic value," while KRAS and NRAS have "relatively strong" evidence as negative predictors of benefit to anti-EGFR therapies. In addition to considerations for specific mutational analysis were recommendations for how laboratories can aid adoption of CRC molecular testing.

- Laboratories should use CRC molecular biomarker testing methods that are able to detect mutations with at least 5% mutant allele frequency.
- Laboratories should optimally utilize tissue specimens by using appropriate techniques (e.g., multiplexed assays).
- Laboratories must use validated CRC molecular biomarker testing methods with sufficient performance characteristics and must incorporate these methods into their overall laboratory quality improvement program.
- CRC molecular biomarker testing reports should include a results and interpretation section easily understandable by oncologists.
- It is suggested that 90% of reports be available within 10 working days from date of receipt in the molecular diagnostics laboratory.
- It is suggested that for laboratories requiring send-out testing, 90% of specimens should be sent out within 3 working days.

Update for Screening for Genital Herpes

An update on screening for genital herpes remains "consistent" with the previous 2005 U.S. Preventive Services Task Force (USPSTF) recommendations against routine serologic screening for genital herpes simplex virus (HSV) infection in asymptomatic adolescents and adults. The update, published in the Dec. 20, 2016 issue of the Journal of the American Medical Association, includes the recommendation to not screen asymptomatic, pregnant women.

"Based on the natural history of HSV infection, its epidemiology, and the available evidence on the accuracy of serologic screening tests, the USPSTF concluded that the harms outweigh the benefits of serologic screening for genital HSV infection," the task force writes.

SPECIAL FOCUS: PEDIATRICS

Sequencing Pediatric Cancer Provides Clinically Useful Information

The Precision in Pediatric Sequencing (PIPseq) Program at Columbia University Medical Center released data on its first 100 patients, which shows that integrating clinical next-generation sequencing (NGS) into pediatric hematology-oncology practice is feasible and has "broad" clinical utility. According to the study published Dec. 23, 2016 in *Genome Medicine*, genomically informed data impacts diagnosis and prognosis, as well as treatment and other significant health maintenance decisions.

> *"While we used a variety of analytical approaches matched to the clinical indications, we primarily utilized a combination of tumor/normal WES and tumor RNA-seq."*
>
> — Andrew Kung, M.D., Ph.D.

The PIPseq program was initiated in 2014 to prospectively integrate NGS into clinical decision making for high-risk pediatric cancer patients. (High-risk patients had a prognosis of less than 50 percent five-year survival, rare cancer without standard of care therapy, suspected cancer predisposition, or relapsed disease.) High-risk patients account for about one-third of the total clinical practice.

The first 101 consecutive participants (mean age, 9.3 years) had a total of 120 samples sequenced between January 2014 and April 2016. Results were initially reviewed by a molecular pathologist and then by a multi-disciplinary molecular tumor board. Clinical reports were issued to the ordering physician and posted to the patient's electronic medical record. Testing included full cancer whole exome sequencing (cWES; tumor, germline, and RNA; n = 63); cWES without RNA (n = 19); RNA only (n = 3); targeted tumor panel sequencing (Columbia Comprehensive Cancer Panel of 467 cancer-associated genes; n = 13); and constitutional WES (proband and parental blood; n = 22).

"While we used a variety of analytical approaches matched to the clinical indications, we primarily utilized a combination of tumor/normal WES and tumor RNA-seq," writes co-senior author Andrew Kung, M.D., Ph.D., from Columbia University (New York). "This platform provided several advantages over targeted cancer gene panels, including the ability to identify translocations, segmental chromosomal changes, and relative gene expression changes."

After filtering, the researchers identified a total of 180 reportable mutations and 20 fusions (110 mutations from solid tumor samples with a mean of 2.91 aberrations per sample and 90 mutations from hematologic samples with a mean of 5.2 aberrations per sample). Potentially actionable alterations were identified in 21 of 65 patients with solid tumors and 17 of 36 patients with hematologic conditions. Yet, only 16 percent of these patients subsequently received matched therapy. The authors say the lack of data in pediatric populations is a known "constraint" to applying targeted therapies in the pediatric setting.

SPECIAL FOCUS: PEDIATRICS

Genomic Data Informs Beyond Targeting Therapy

"Beyond the identification of actionable alterations, the ability to avoid ineffective/inappropriate therapies, make a definitive diagnosis, and identify pharmacogenomic modifiers is clinically impactful," the authors write.

"Non-targetable" genomic alterations identified through sequencing provided a molecular diagnosis in 23 patients and identified prognostic, pharmacogenomic, and other significant health maintenance recommendations in 32 patients. RNA sequencing and copy number variant analysis yielded clinically impactful data, beyond identification of therapeutic targets, in 23 of 33 patients.

Known or likely pathogenic germline alterations were discovered in 20 percent of patients, with 14 percent having germline alterations in cancer predisposition genes. American College of Medical Genetics and Genomics findings were identified in six patients and were returned to the families. The authors say this is a higher rate than other studies have identified, even in pediatric populations, and underscores the need to "routinely" utilize germline analysis in pediatric oncology.

"We believe that narrowing the definition of benefit to the identification of actionable targets and matched targeted therapy underestimates the potential clinical utility of comprehensive genomic analysis," Kung and colleagues write. "Taking a more inclusive view of potential clinical utility, 66 percent of cases tested through our program had clinically impactful findings and samples interrogated with both WES and RNA-seq resulted in data that impacted clinical decisions in 75 percent of cases."

The total cost per case (the sum of the total variable cost [e.g., reagent cost, pathologist time] plus the fixed cost per case [e.g., annual machine cost, annual maintenance, tech labor cost, informatics cost, space for NGS hardware, server time, NGS analysis lease, and data storage]) was estimated to

Sequencing Also Showing Utility in Pediatric Brain Tumors

The combination of NGS and copy number profiling can identify critical diagnostic, prognostic, and treatment-relevant alterations in the assessment of pediatric brain tumors, according to a study published Jan. 19 in *Neuro-Oncology*.

Profile, a prospective, personalized medicine, clinical research initiative at Dana-Farber Cancer Institute (Boston), uses OncoPanel, a multiplexed targeted exome-sequencing platform (300 cancer-causing genes) to identify single nucleotide variants and rearrangements/indels. Additionally, OncoCopy, a clinical genome-wide array comparative genomic hybridization assay evaluated copy number alterations and was better able to define rearrangement breakpoints.

In the present study, cancer genomes from 203 pediatric brain tumor patients (median age, 8 years) were profiled (January 2013 and June 2015) across histological subtypes. The OncoPanel analyzed 117 samples, OncoCopy 146, and 60 tumor samples were assessed using both methodologies.

OncoPanel identified clinically relevant alterations in 56 percent of patients (44 cancer mutations and 20 rearrangements), including BRAF alterations that enabled use of targeted therapies. Copy number profiles differed across histologies.

"Our finding that copy number profiles broadly differ between embryonal and glial lineages holds the potential to further improve accuracy and reproducibility of diagnostics, particularly as increased numbers of tumors are profiled," write the authors led by Shakti Ramkissoon, M.D., Ph.D., from Dana-Farber/Boston Children's Cancer and Blood Disorder Center. "We believe that leveraging these findings provides a more clinically useful route to tumor classification."

SPECIAL FOCUS: PEDIATRICS

> *"The value proposition for next generation diagnostics, therefore, should be measured both on the clinical impact of the data and the ability to replace multiple conventional single endpoint assays with a single comprehensive view of the genome."*
>
> — Andrew Kung, M.D., Ph.D.

be $4,459 for WES (tumor/normal) and $1,764 for RNA-seq. These estimates do not include administrative overhead and billing for services.

Additionally, the researchers share that the time to receiving final reimbursement decisions from third-party payers ranged from 6 months to 1 year. As of publication, reimbursement decisions were received for 56 patients with 80 percent receiving partial reimbursement. The average reimbursement was $2,747 for commercial plans, $2,918 for managed government plans, and $0 from government plans.

"The value proposition for next generation diagnostics, therefore, should be measured both on the clinical impact of the data and the ability to replace multiple conventional single endpoint assays with a single comprehensive view of the genome," the authors suggest.

Takeaway: The PIPseq program shows early evidence that a clinical pediatric hematology-oncology sequencing program is not only feasible, but offers a wide-range of clinical benefits.

Blood-based, Proteomic Test May ID Preterm Delivery Risk, Saving Infant Lives, Costs

The use of a novel test for identifying pregnant women at risk of spontaneous preterm birth risk could improve infant outcomes and reduce the overall economic impact of preterm birth, according to a study published in the December 2016 issue of the *American Journal of Perinatology Reports*.

The PreTRM test by Sera Prognostics (Salt Lake City) analyzes maternal blood using liquid chromatography-tandem mass spectrometry as early as 19 weeks of gestation. The proteomic test simultaneously measures multiple proteins associated with preterm birth, including those tied to inflammation, hemorrhage, stress, and uterine over-distention. The test developers say that identifying women at risk for premature delivery enables individualized and informed clinical care.

Approximately one in 10 babies born in the United States is premature (born before 37 weeks gestation), which is associated with a significantly increased risk of major long-term medical complications, including learning disabilities, cerebral palsy, chronic respiratory illness, intellectual disability, seizures, and vision and hearing loss. These complications are costly, estimated to be an average of $54,194 in medical cost per preterm baby (roughly 10 times the cost for a full-term baby).

The researchers found that the model predicted a 23.5 percent reduction in infant mortality (approximately 2,000 fewer neonatal deaths per year) with use of the novel test.

In the present study, the researchers developed a decision-analytic model to assess clinical and cost outcomes over a one-year period based a hypothetical population of 3,528,593 pregnant women with a singleton gestation and no history of spontaneous preterm birth. The PreTRM test was hypothetically applied to women in the predictive arm and compared to a hypothetical cohort using the current standard of care and baseline rates of spontaneous preterm birth and associated infant morbidity and mortality (baseline care arm). The model assumed 80 percent for both test sensitivity and specificity, as well as a $1,250 cost for the test (based upon cost for noninvasive prenatal testing at launch).

The researchers found that the model predicted a 23.5 percent reduction in infant mortality (approximately 2,000 fewer neonatal deaths per year) with use of the novel test. The rate of acute conditions at birth decreased from 11.2 percent to 8.1 percent. Similarly, the rate of developmental disabilities decreased from 13.2 percent to 11.5 percent. The rate of spontaneous preterm birth decreased from 9.8 percent to 9.1 percent, translating to roughly 23,430 preterm births. On average, 6.8 percent of births that would have been preterm in the baseline arm shifted to full term in the predictive arm.

Additionally, the researchers identified a direct medical cost savings of $511.7 million, a decline of 2.1 percent during the first year of life. The cost-benefit analysis demonstrated overall total cost savings (direct and total costs) of $1.49B through hypothetical use of the test in the predictive arm. These direct medical cost savings were realized due to a decrease in hospitalization and rehospitalization costs resulting from increasing the average gestational age.

Takeaway: A novel, proteomic blood test may identify women at increased risk of spontaneous, preterm delivery. Through identification of these women and early intervention, improvements in infant outcomes and costs may be achieved.

Study Shows Benefits of Large-Scale, Clinical Sequencing Initiatives

Large-scale sequencing initiatives performed in integrated health care systems, such as the DiscovEHR collaboration, can advance genetic discovery and serve as a "blueprint" for adoption of precision medicine, according to a study published Dec. 23, 2016 in *Science*.

The DiscovEHR study is a collaboration between the Regeneron Genetics Center (wholly-owned subsidiary of Regeneron Pharmaceuticals) and Geisinger Health System (Danville, Penn.). The initiative couples high-throughput sequencing and longitudinal electronic health records (EHRs) in a real-life clinical cohort that enables returning and acting on reportable variants.

Sequencing of the exomes of 50,726 adult participants in the DiscovEHR study (sequence coverage of at least 20× haploid read depth at more than

85 percent of targeted bases in 96 percent of samples) identified roughly 4.2 million rare, single-nucleotide variants and insertion/deletion events, of which approximately 176,000 predicted a loss of gene function. Each individual had a median of 21 rare variants predicted to result in a loss of gene function.

"Although many of these variants are rare individually, in aggregate, they are not uncommon, and their identification and the biological insights gleaned are relevant to our understanding and treatment of both common and rare diseases."

— David Carey, Ph.D.

The researchers found that linking these data to EHR-derived clinical phenotypes for more than 39,000 patients, uncovered associations supporting therapeutic targets, including genes encoding drug targets for lipid lowering, and identified previously unidentified rare alleles associated with lipid levels. Clinical records covered a median of 14 years and captured a median of 87 clinical encounters, 658 laboratory tests, and seven procedures per participant.

During consent, participants agreed to be recontacted for return of clinically actionable results to inform their health care. The researchers found that roughly 3.5 percent of individuals harbored deleterious variants in 76 clinically actionable genes and potentially pathogenic variants known as the Geisinger-76, which include the 56 genes and 25 conditions recognized in the American College of Medical Genetics and Genomics reporting recommendations plus an additional 17 genes associated with the same 25 conditions and three genes associated with two additional conditions.

Following expert clinical review and adjudication of potentially pathogenic variants, 43 reportable variants (all either heterozygous for autosomal dominant conditions or hemizygous for X-linked conditions) were identified in 49 individuals. The expressivity of these variants were investigated through reviewing EHR-derived clinical phenotype data for variant carriers. Nearly two-thirds (32 of 49 individuals) had documented clinical features in the EHR consistent with the associated disease, however only seven individuals (14 percent) had a formal diagnosis of the associated disease. Geisinger has stated that for the 200 patients already informed they carry one or more actionable, disease-causing genetic mutations, most variants are related to cancer risk and cardiovascular illness.

"Although many of these variants are rare individually, in aggregate, they are not uncommon, and their identification and the biological insights gleaned are relevant to our understanding and treatment of both common and rare diseases," writes senior author David Carey, Ph.D., from Geisinger Health System, in the study. "These results demonstrate the potential for genomics-guided clinical care in a large unselected clinical population, establish an expectation for the burden of actionable genetic findings, and support the need for expert clinical review and adjudication of assertions of pathogenicity for potentially pathogenic variants, including those cataloged in mutation databases."

Takeaway: Large-scale sequencing initiatives linked to clinical data can inform the practice of precision medicine and drive genomics-guided therapeutic discovery.

Many Breast Cancer Patients Not Referred for Genetic Testing, *from page 1*

Women (aged 20 to 79 years) diagnosed with breast cancer (stages 0 to II) between July 2013 and September 2014 were identified using the Surveillance Epidemiology and End Results registries of Georgia and Los Angeles County. Identified women were mailed surveys two months after surgery. Questions assessed patients' desire for genetic testing (not at all, a little bit, somewhat, quite a bit, very much), whether patients talked about testing with any "doctor or other health professional," had a session with a genetic counseling expert, or completed testing. Cancer family history, ancestry, and clinical information were also assessed to gauge a guideline-concordant measure of high pretest risk for mutations.

"It is likely that some doctors don't realize the benefit that genetic testing provides. They may also lack the ability to explain the testing process and results clearly with patients. Priorities for the future should include strategies to expand the genetic counselor workforce and interventions to improve physicians' skills in communication and cancer risk assessment."

— Allison Kurian, M.D., Stanford Cancer Institute

Based on the 2,529 women (mean age 62 years; 56.8 percent white) who responded to the survey, overall, 66 percent reported wanting testing, but only 29.0 percent reported having a test. Asian-Americans and older women were more likely to be undertested, but in this population education, income, and insurance status did not affect testing rates.

Among average-risk patients, 59.3 percent wanted testing, 35.9 percent reported talking about testing with a doctor or other health professional, and 17.8 percent had a test. Nearly one-third of women (31 percent) had a high pretest mutation risk. Among high-risk patients, 80.9 percent wanted testing, 70.9 percent talked about testing with a doctor or other health professional, 39.6 percent had a session with a genetic counseling expert, and 52.9 percent had testing. Among tested, high-risk patients, more (61.7 percent) reported having a genetic counseling session.

The 47 percent of high-risk patients not having a genetic test represents a "missed opportunity," the authors say, to prevent other cancers in mutation carriers and their families. The most common reasons high-risk patients reported for not testing were "my doctor didn't recommend it" (56.1 percent), "too expensive" (13.7 percent), and "I did not want it" (10.7 percent).

"It is likely that some doctors don't realize the benefit that genetic testing provides," says co-senior author Allison Kurian, M.D., from the Stanford Cancer Institute. "They may also lack the ability to explain the testing process and results clearly with patients. Priorities for the future should include strategies to expand the genetic counselor workforce and interventions to improve physicians' skills in communication and cancer risk assessment."

Takeaway: Rates of genetic testing among women diagnosed with breast cancer remain low, despite their self-reported desire for testing. Given this gap, there is a need for increased education of physicians regarding risk assessment and the need for genetic testing, combined with expanded triage to genetic counselors.

Nurses Seeking to Advance Genomics Understanding

The case has been made repeatedly over the past few years regarding the need to increase physicians' genomics knowledge. Now, for the first time, there are efforts underway to establish a global genomics nursing alliance to advance genomics in routine nursing practice.

The Global Genomics Nursing Alliance (G2NA) project says that nurses have a pivotal role in bringing the benefits of genomics to everyday health care. To do this, they say, a global effort is needed to transform nursing policy, practice, education and research.

"Embracing genomic healthcare requires a prepared workforce that can inform, educate and empower people," Kathleen Calzone, from the U.S. National Cancer Institute told delegates at a three-day summit held at the Wellcome Genome Campus in the United Kingdom (Jan. 22-25). "This represents a significant challenge as deficits in nurses' knowledge and skills in genomics are widely acknowledged."

The summit delegates agreed to focus action in the core areas of improving education and workforce development, collaborating and communicating across borders and professional groups, and transforming health care through policy development. G2NA will also develop a Roadmap that will enable nurses to assess their organization's genomics development, compared to national and sub-national benchmarks; share a nursing resource toolkit on genetics, and establish partnerships for consultation and collaboration.